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Table of Contents.

The Edward Stirling Lectures.[1]

LECTURE I: TUMOURS OF THE ALVEOLAR PROCESSES.

By R. KAYE SCOTT, M.D., M.S. (Melbourne), F.R.A.C.S., F.F.R., F.C.R.A., D.T.R.E. (Melbourne),
Melbourne.

PROLOGUE.

EDWARD CHARLES STIRLING was born in 1848 at Strathalbyn, and received his schooling at St. Peter's. Winning the Westminster Scholarship, he went to Trinity College, Cambridge, and successively gained his B.A., M.A., M.R.C.S., M.B., F.R.C.S. and M.D. qualifications. He returned to South Australia in 1881, having had post-graduate teaching and surgical experience. He soon embarked on an academic career, though for a considerable time he retained a major interest in surgery. He was appointed lecturer and later professor of physiology in the University of Adelaide.

He served the community well and faithfully. He became President of the South Australian Branch of the British Medical Association; he was for many years a member of the Council of the University of Adelaide, and he was Dean of the Faculty of Medicine for eleven years. Probably no one did more than he to guide and shape the destiny of the developing medical school of this university.

It is now thirty-six years since his death, and so only the senior members of the university will remember him. We all like to look in retrospect at the days of our schooling, our studenthood and our post-graduate apprenticeships. We can each recall a small and select group of men who loom large on our individual horizons, men who were of great mental stature, men who had ability to teach and who impressed their characters on our youthful plastic minds. Those who knew him will surely count Stirling as such a man. Tonight you and I are gathered here to honour his name, and I in humility approach the task of delivering his memorial lectures, well realizing the responsibility which has fallen on me.

TUMOURS OF THE ALVEOLAR PROCESSES.[1]

The chief purpose of this paper is the presentation of a classification of the tumefactions arising in the dental alveolus in association with dental structures. It is impossible to consider the dental tumours without discussing those of bone proper, and so the subject really becomes tumours of the maxilla and mandible.

The epithelial downgrowths of the dental ridge are in such intimate relationship with the mesenchyme of the

[1] Delivered on May 31 and June 2, 1955, at Adelaide.

[1] Dr. Kaye Scott illustrated his lecture with lantern slides showing photomicrographs of histological sections, clinical photographs and reproductions of X-ray films of illustrative patients.

alveolar bone that the dental group of tumours are in reality epithelial organoid tumours of bone. These, together with similar organoid tumours, arising for example in the pituitary region, legitimately constitute one of the main subdivisions of the primary tumours of bone.

If the subject of the special alveolar tumour is approached from the point of view of tumours of the mandible and maxilla, the following general classification is offered:

A. *Natural tumours of bone*:
   Innocent tumours.
   Malignant tumours.

B. *Site predisposition to direct involvement by contiguous extrinsic neoplasms*:
   Innocent: "Dental fibroma", angioma *et cetera*.
   Malignant: Invasion by tumours originating, for example, in antrum, mouth, lip, cheek or salivary glands; or secondary carcinomatous glands of the neck.

C. *General predisposition to blood-borne metastases from distant neoplasms*:
   For example, secondary spread from the breast, lung, kidney or any other primary neoplasm.

D. *Odontomes*: *Special alveolar tumours of dental origin*:
   Central tumours within the alveolar process.
   Outgrowth tumours upon the process: true epulides.

Natural Tumours of Bone.

Among the natural tumours of bone, common innocent tumours are fibroma, chondroma, osteoma and benign giant-cell tumour. The malignant tumours are osteogenic sarcoma, malignant giant-cell tumour, and malignant tumours of marrow—that is, those of reticulo-endothelial origin.

The mandible and maxilla differ little from other bones which have been developed essentially as membrane bones, and so the usual range of innocent tumours may be encountered, as set out above. Fibroma of non-osteogenic type occurs in the long bones, but is excessively rare in the mandible and maxilla, if the condition of *osteitis fibrosa*, which is extremely common in those bones, is excluded. Similarly, a chondroma would be a most unexpected tumour in mandible or maxilla. In the absence of a major growing epiphysis, osteoma is much less frequent than in long bones, and only the periosteal types of osteoma are likely to be seen. New bone is laid down under the periosteum, and an ivory or compact osteoma results. Sometimes moulding may occur beneath the newly laid down layers, with formation of cancellous bone under the new subperiosteal bone forming a periosteal cancellous osteoma.

Giant-cell tumours are of various types; the giant-cell tumours of tendon sheath, those tumours associated with calcium resorption in hyperparathyroidism, the tumour found in long bones under the epiphysis and the giant-cell tumour arising near tooth sockets may be mentioned. In all these tumours the osteoclast, or more properly its mononuclear precursor, is regarded as the histogenetic component. In the absence of an epiphysis in the body of the mandible, it is very doubtful whether giant-cell tumours ever originate in the maxillary or mandibular bodies. Their appearance in these bones is limited to the alveolar processes where they arise in association with tooth structures, and invasion into the main mass of either bone is always through alveolar bone. Alveolar bone giant-cell tumours therefore are regarded in this site as special tumours of dental tissues—that is, odontomes in the sense now defined. Subepiphyseal giant-cell tumours such as occur in cartilage bones do not occur primarily in mandible or maxilla.

For the purpose of this discussion it is possible to restrict consideration of the malignant tumours of ordinary bone to four representative types—osteogenic sarcoma, malignant giant-cell tumour, Ewing's tumour and multiple myeloma.

Osteogenic sarcoma is commonest in the long bones, but may occur in any bone. Its appearance in the mandible and maxilla is rare, and very few cases of true osteogenic sarcoma of the mandible are on record. It is understood that such a tumour would arise in bone-formative tissues, and so would have capacity for formation of neoplastic bone, cartilage, fibrous or myxoid tissues according to the degree of differentiation exhibited. The body of the bone being relatively larger than the alveolar processes, one would expect such tumours to occur more frequently in the body. In this situation osteogenic sarcomata in the mandible are excessively rare, but they are a little more frequent in the body of the maxilla. Osteosarcoma—that is, the bone-productive variety of osteogenic sarcoma—is almost unknown in the alveolar processes.

But there is a not uncommon sarcoma of fibrosarcoma type appearing in the alveolus, either as an invasive or as an exophytic tumour. Erosion of the alveolar processes readily occurs, whence spread takes place into the body of the bone. This tumour never exhibits neoplastic bone or cartilage formation and is regarded as a primary tumour of dental tissue origin and therefore as an odontome.

Examples of chondrosarcoma occurring in the mandible or maxilla have been reported in the recent literature (Miles, 1950), and one of these has been seen recently. The neoplasm forms a fairly pure cartilage matrix with no tendency to bone or osteoid formation, though dedifferentiation readily occurs. The tumours are therefore similar to the chondrosarcomatous neoplasms of pelvis, humerus and the flat cartilage bones, and therefore are properly included in the osteogenic sarcoma series. There is no reason to believe that they are specially alveolar in site or dental in origin. Spread of the tumour to regional glands was a striking feature of our case.

Just as alveolar giant-cell tumours of benign type are common, so malignant varieties of this tumour may occur. But they also are of dental and not "general bone" origin; such tumours have not been found primarily in the bodies of the bones.

Ewing's tumour and multiple myeloma are not infrequently found in the state of generalization of the diseases in the maxilla or mandible; one would not expect to encounter such tumours originating in such sites.

Site Predisposition to Direct Involvement by Contiguous Extrinsic Neoplasms.

In relation to predisposition to direct involvement by contiguous extrinsic neoplasms, the following classification may be used: (i) innocent tumours—for example, papilloma, angioma, dermoid cyst, "dental fibroma"; (ii) malignant tumours—for example, carcinoma of the antrum, the buccal mucosa and tonsil, the skin of the cheek, and the salivary glands (parotid and submaxillary), secondary carcinoma in the submaxillary or upper cervical lymph glands, and, rarely, other malignant tumours.

Any bone is liable to invasion by malignant tumours arising in or involving adjacent tissues. The maxilla and the mandible are liable to invasion by a great variety of tumours on account of the diversity of tissues which have relation to them. The direct invasion of bone by an extrinsic neoplasm is of no extraordinary interest; in this situation it is the diversity of causes which justifies examination.

The alveolar processes are particularly the portions of these bones in which we have interest.

Innocent tumours may be found on the tissues overlying these processes and are rarely of importance. Examples of simple papillomata, angiomata of infancy and salivary tumours of buccal gland origin may be quoted; a mid-line dermoid cyst overlying the upper anterior process was wrongly diagnosed as a salivary tumour in one of my cases.

A very common tumefaction of the perialveolar soft tissues is caused by an ill-fitting artificial denture. The friction causes epithelial irritation, fibrosis of the subjacent tissues follows, and the fibrotic plaque is initially covered by a smooth epithelium and perhaps grooved by the denture. Sooner or later friction causes ulceration and sepsis supervenes. Œdema causes swelling and perhaps subjacent abscess follows. Often the inflammation causes another groove to be made by the denture in the swollen tissues, and from a simple fibrotic plaque a most irregular and inflamed corrugated tumour of considerable size may arise from the alveolar margin.

The inflammation associated with the tissue hyperplasia has caused many such tumefactions to be diagnosed as carcinomatous. The naming of this entity has caused trouble—originally called a "dental papilloma", it is neither papillomatous nor always dental. The now generally accepted designation, "prosthetic fibrosis", does not adequately indicate the degree of tumefaction which may be present.

Other examples of innocent tumours could be quoted —none is of importance.

Carcinoma arising within the antrum may involve the bone and present into the mouth, either lateral to the alveolar process by eroding through this bone, or by infiltrating through the palate.

Squamous carcinoma originating or spreading on to the alveolar mucosa may readily invade subjacent bone.

Invasive neoplasms of either basal or squamous type, of cutaneous origin, not infrequently involve the alveolar processes from the face.

Carcinoma arising in either the parotid or submaxillary salivary glands may involve the mandible, while destruction of the bone from secondary carcinomatous submandibular glands is not common.

These examples by no means exhaust the list of possibilities.

General Predisposition to Blood-Borne Metastases from Distant Neoplasms.

Tumours in the third section of the classification may be set out as follows: secondary tumours from carcinoma of the breast, carcinoma of the lung, carcinoma of the kidney, or any other primary neoplasm.

Blood-spread secondary deposits are most common in red marrow-containing bones—vertebræ, pelvis, skull, upper ends of humeri and femora. Deposits are not common in the mandible or maxilla at an early stage of bony dissemination, though involvement of these bones is not uncommon when sowing is widespread in late stages of the disease. Involvement of the alveolar processes is still less common. Some striking examples of blood-spread deposits have been seen and are shown as pathological curiosities. Naturally, any tumour which has invaded vascular channels may form an alveolar metastasis. As an example, a carcinoma of the breast forming an alveolar nodule has been seen. The body of the mandible may more often be involved.

Another patient reported with the complaint of ulceration and swelling involving the posterior left lower alveolar process, and examination revealed external swelling of the body of the mandible. There was no complaint of symptoms other than loss of weight. A secondary tumour was suspected, lung signs were found to be present, and radiological examination revealed appearances suggesting a primary carcinoma of the lung and secondary invasion of the mandible. Biopsy from the area of alveolar ulceration showed "carcinoma". Here the alveolar ulceration and swelling were the first symptoms of a carcinoma of the lung.

An alveolar metastasis from a retinoblastoma constituted another pathological rarity.

This child had had her right eye removad, and two and a half years later was sent down from the country with swelling involving the fibula, with X-ray appearances suggesting Ewing's tumour. Aspiration biopsy revealed tissue of neuroblastomatous type. Later a metastasis in the alveolar process caused displacement of teeth and local swelling, and subsequently generalized bony deposits appeared.

Special Alveolar Tumours of Dental Origin.

The special alveolar tumours of dental origin may be classified as follows: (i) epithelial odontomes: primary tumours of dental epithelium; (ii) composite odontomes: tumours containing tissues of both epidermoid and mesenchymal variety; (iii) mesenchymal odontomes: tumours consisting solely of connective tissue elements—(*a*) central alveolar tumours, (*b*) outgrowth group (true epulides).

Teeth develop from downgrowths of the alveolar epithelium about which condensations of mesenchymal tissue occur, so that both types of tissue play an integrated part in the formation of the teeth. Malassez (1885, quoted by Ewing, 1940) described numerous groups of epithelial cells lying between the developing teeth and probably derived from the epithelial downgrowths of the dental ridge, but not taking part in the formation of the normal teeth.

In general, confusion surrounds the terminology of tumours arising from tooth structures. The problem is made infinitely more difficult because there is no clear delineation between true neoplasms, developmental abnormalities forming tumefactions, and inflammatory processes of hyperplastic or destructive type.

It is therefore wise for us to consider together all those processes which form clinical tumefactions, be they neoplasms, maldevelopments or inflammations. A classification is of value only when it clarifies our ideas and allows us to define recognizable entities. It can never be unchangeable and must be revised from time to time to keep in line with changing pathological and embryological concepts.

Bland-Sutton (1906) long ago defined an odontome as a tumour "composed of dental tissues in varying proportions and different degrees of development arising from teeth germs, or teeth still in the process of growth". He then described various types of odontomes including "epithelial odontomata" from the enamel organ, "fibrous odontomata" from the tooth follicle and "composite odontomata" from the whole germ.

Later writers (for example, Willis, 1948) have tended to restrict the term odontome to describe solely those tumefactions of composite type involving enamel dentine and cement structures and so of mixed epithelial and mesenchymal origin.

I think it much wiser to return to the broader ideas of Bland-Sutton and follow his principles and extend his classification in accordance with later pathological developments.

An odontome can now be defined simply as any tumour arising from dental tissues. We can immediately subclassify all such tumours into a group in which the epithelial elements predominate—epithelial odontomes. A second group contains the composite odontomes comprising tumour elements of both epidermal and mesenchymal tissues; and tumefactions arising in dental mesenchymal tissue, particularly the periodontal membrane, fall naturally into a third group of mesenchymal odontomes.

At this stage the term "epulis" must be considered. It is generally descriptive of any outgrowth from the alveolar process, being derived from the Greek (*ἐπί*, upon, *οὖλον*, the gum). This term is used by many writers and clinicians purely in its original descriptive sense, and unfortunately this use is likely to persist. Most authorities limit its use to those tumours arising from the mesenchymal peridental tissues, and so make of it a specific dental tumour (Amies, 1951).

The only way in which these usages can be correlated is to suggest that the dental group of tumours be called "true" epulides, and that other tumefactions of extrinsic origin appearing on the alveolar processes be classed as "false" epulides.

Just as a carcinoma originating on a surface may be of fungating or ulcerating variety representing outgrowth and ingrowth types, so a tumour arising in the periodontal membrane may form a tumour fungating from the gum which is an epulis, or a central alveolar tumefaction if its tendencies are invasive. In this analysis a true epulis is therefore a special case of a mesenchymal odontome.

Epithelial Odontomes.

Epithelial odontomes may be classified as follows: (*a*) dental cysts, (*b*) dentigerous cysts, (*c*) true epithelial odontomes; benign: multilocular cystic disease (or benign epithelial odontome); malignant: basal-cell type—adamantinoma; squamous-type — intraalveolar epidermoid carcinoma.

If an odontome is defined as a tumour arising from dental tissues, then any such tumefaction in which epithelium forms a major part must be considered among the subclass of epithelial odontomes.

This group then includes some inflammatory conditions, some developmental abnormalities and some innocent or malignant neoplasms. The line of demarcation between these varieties is exceedingly tenuous. All are tumours in the broad sense, and as such the clinician must deal with them. The last word as to their classification must be left to the pathologist.

Dental cysts and dentigerous cysts are in the non-neoplastic class. Any inflammation may be suppurative or non-suppurative; either may be localized or diffuse. A localized inflammation may therefore, if it is suppurative, form an abscess cavity, or if it is non-suppurative may progress to destruction of bone with formation of granulation tissue with defined or ill-defined border.

Abscess cavities so formed in relation to tooth roots may be of long standing and their content is often sterile. Such cavities are frequently found with a complete or partial epithelial lining, the epithelium is usually columnar or stratified, wide variation in epithelial form may be encountered, and a not uncommon feature is the departure from appearances of typical oral stratified epithelium.

Up to the present practically all authorities ascribe the epithelium to remnants of the Malassez cells known to be present in the peridental regions (Bland-Sutton, 1906; Ewing, 1940; Willis, 1948; Scudder, 1912; Worth, 1937). It is believed that the epithelial lining in some of the cases is metaplastic in origin.

Dentigerous cysts may involve a permanent tooth in its normal site of alveolar development, but occasionally a dentigerous cyst is found in a site remote from that at which normal teeth grow—for example, the hard palate. All these dentigerous cysts have as a common feature a tooth wholly or partially within the wall of the cyst, which originally had epithelial lining derived from the enamel organ. The cyst in an abnormal site represents a maldevelopment, perhaps even a very highly specialized innocent tumour, formed from a downgrowth of oral epithelium. It must be compared with a tooth-containing dermoid cyst, and has claims to be considered a real neoplasm.

On the other hand, many of the dentigerous cysts occurring at the normal sites of tooth development represent the end result of infections reaching the developing permanent tooth germ from the overlying milk tooth. Though the two types of cyst appear identical, sharp pathological distinction must be drawn between them.

Multilocular cystic disease of the jaw, better described as benign epithelial odontome, can be classified either as a malformation or as an innocent neoplasm. Four cases are in my series, two from each of two families. The body and perhaps ramus of the mandible are found expanded by multiple cyst-like cavities, and the dentition is imperfect, with some missing teeth. It is assumed that the dental ridge epithelium has developed imperfectly and that some tooth germs have not formed. The epithelium has continued to grow widely into the bone, forming initially multiple epithelial-lined cysts, which later become filled with epithelial debris and cholesterol crystals. The destruction of bone is accompanied by a giant-cell tissue proliferation, and the presence of this tissue, which may overgrow the epithelial tissues, has resulted in the improper recognition of this pathological entity in the past. In the first of my cases the condition was diagnosed on biopsy as giant-cell tumour of the mandible, and the true nature of the disease was not recognized until the patient's younger brother became affected.

The epithelium is unstable. In my last two cases the disease has responded to quite small doses of X-ray therapy slowly administered, with restoration of bony contour and near normal development of the remaining teeth and mandible. The hereditary nature of the disease in these two families is striking.

Jones (1933 and 1938) described the condition in three children of one family, and also another case of familial multilocular cystic disease of the jaw appearing in the fifth generation known to be affected. The patients exhibited deficient dentition, ballooning of the body and ramus of the mandible and sinus catarrh of submandibular glands. He concludes that the cysts represent an abortive attempt at multiple formation of teeth—the tooth buds degenerate and cysts are produced. Jones adduces no histological study of changes occurring, but shows excellent radiographs, and clearly has in mind that the condition is an abnormal development of the dental ridge downgrowths and normal tooth germs.

The malignant epithelial odontomes include a group of tumours arising from epithelium of dental ridge origin, which therefore may be either epithelium of tooth germs, or persisting remnants of the ridge lying between the germs proper and designated as "Malassez debris". At its limit of differentiation this epithelium forms a structure resembling enamel organ, though practically never real enamel, and the tumour is designated "adamantinoma". As an attempt is being made to produce an appendage structure—namely, a tooth—it is a basal-cell carcinoma behaving in all characteristics as other basal-cell carcinomata, growing by invasion and not metastasizing to lymph glands.

The dental ridge epithelium alternatively may form a squamous-cell carcinoma of differentiated type with prickle cells or keratin, or it may be more anaplastic. This tumour produces those types of cells forming the covering or protective layers and so is a squamous-cell carcinoma; it grows locally and readily metastasizes to lymph glands. Willis (1948) aptly names this group "intra-alveolar epidermoid carcinoma". The capacity of the dental ridge epithelium to form carcinomata of both basal and squamous type is noteworthy and most interesting.

The clinical behaviour of the adamantinoma group is well known. The tumour commences in an intraalveolar situation, grows slowly and infiltrates remorselessly, invading and destroying all tissues in its path. It has a tendency to cause ballooning of invaded bone, and huge tumour masses may result. Its invasive characteristics make the risks of recurrence very great unless well-planned, radical methods of treatment are instituted. Its slow rate of growth may be compatible with survival of the patient with recurrences thirty years after initial treatment, the tumour extending into the zygoma, orbit, temporal fossa or base of the skull.

Early diagnosis of a small adamantinoma may be a matter of great difficulty, and exploration and biopsy may be essential to establish its identity.

Three characteristic radiological patterns are seen in films of these tumours.

The lytic or destructive picture may be present in small or large tumours where infiltration and tumour formation cause ballooning of the tissues and destroy invaded bone, leaving the barest of bone outlines within the soft-tissue mass.

The clinical picture of a massive nodular tumour is often associated with a radiological picture of bone expansion and some new bone formation by residual bony tissue; this, with the regions of multifocal growth, produces the characteristic multilocular appearance.

The third type is a further stage of development of the former multilocular group. The isolated loculi of tumour growth are well seen, but are separated by wide zones of ossific stroma. There is no evidence that this is due to any enamel or like production by tumour tissue. The neoplasm is growing but slowly, and the expanded bone has time to lay down a dense matrix around the tumour loculi. This variety is described as the "honeycomb" type.

The histological picture of adamantinoma is classical; the tumour represents the production of appendages of epidermoid epithelium and so a basal-cell carcinoma is produced; here the cells form alveolar masses lined by tall columnar cells representing the enameloblasts, and the central cells lack intercellular bridges and are referred to as reticular cells. Production of enamel or like substance is most rare.

The normal potentialities of epithelial downgrowths from skin or mucous membranes cover a wide range—sweat glands, sebaceous glands, hair, nails, salivary and wax glands and teeth may be mentioned. Thus we may find

adamantinoma-like appearances in basal-cell carcinomatous tumours originating anywhere within the mouth, and alternately gland formations of one or another type may be seen in tumours apparently arising from dental ridge downgrowths. These constitute the "adenoid" varieties of adamantinoma.

These same cells, instead of forming appendage structures, may exhibit other characteristics of their parent Malpighian cells and form a neoplasm of epidermoid type as already referred to, and a true squamous-cell carcinoma can originate in the intraalveolar tissues as distinct from the overlying mucous membrane. Clinically, one is convinced of this entity, aptly named intraalveolar epidermoid carcinoma, when in a young man in the third or fourth decade a squamous carcinoma presents in the alveolar process from below the mucous membrane and subsequently ulcerates. It is easy to understand cells of Malassez debris surviving into early adult life; but conditions alleged to be of this type in the elderly patient must be looked upon with suspicion. Here well-recognized chronic irritations will usually be found which will explain the genesis of the growth.

Composite Odontomes.

Composite odontomes may be classified as follows: (i) complex—irregular solid masses of enamel dentine and cement in a fibrous capsule; (ii) compound—multiple masses with separate capsules, each representing an individual tooth; (iii) geminated—a mass consisting of two or more fused teeth; (iv) dilated—the tooth structure is ballooned into a cyst-like mass; (v) gestant—*dens in dente.*

Composite odontomes are tumours containing both epithelial and mesenchymal elements. In some groups tooth development to a considerable state of maturity has taken place. At one extremity are a group of frank maldevelopments, merging at the other end to tumour masses which might be considered as innocent neoplasms. It is necessary to exclude from the group many varieties of tumefactions in which highly organized inflammatory tissues around a tooth form an abnormal mass. Cementomata and fibrous and radicular odontomes as described by Bland-Sutton (1906) probably fall within this exclusion.

Worth (1937) described four varieties of composite odontomes; it is not necessary to depart from his classification.

Complex composite odontomes are comprised of irregular solid masses made up of enamel dentine and sometimes cement, and the whole mass is enveloped by a mesenchymal condensation representing the periodontal membrane, which shows radiologically as a radiolucent capsule.

Compound composite odontomes are composed of multiple discrete masses of similar type and differ from the complex odontome in that each mass has a separate connective tissue capsule often incomplete, the whole enclosed in one large outer membrane. Radiologically this fragmentation is characteristic and probably represents multiple individual teeth, each with its own periodontal membrane. These new teeth may reach considerable perfection of development. Tumours of this type have been described by Bland-Sutton (1906) containing hundreds of tiny teeth.

The geminated odontome is composed of a crown mass belonging to two or three fused teeth, each with its distinct and separate roots. It would appear to be a frank malformation.

The dilated composite odontome shows a normal crown structure superimposed upon a cyst-like mass, around the margins of which root structures may be seen. One suspects an inflammatory process occurring somewhere in the mesenchymal tissues of the dental papilla at a late stage in tooth development—a stage when the crown with its enamel has been well formed, but before the full development of root structures has occurred. The "dilated" odontome is probably not a tumour or even a malformation.

The gestant odontome is due to an invagination of dental elements, so that an inverted tooth is formed within the original tooth.

Mesenchymal Odontomes.

Tumours arising from mesenchymal periodontal tissues may be classified as follows:

Central alveolar variety:
- (i) Osteoclastoma: innocent giant-cell tumour; malignant giant-cell tumour.
- (ii) Fibroid types: innocent: (*a*) granuloma—solid or cystic, (*b*) hæmangioma, (*c*) *osteitis fibrosa* —localized variety, spreading variety, diffuse variety; malignant: alveolar fibrosarcoma.

Outgrowth variety true epulides:
- (i) Osteoclastoma: innocent giant-cell tumour; malignant giant-cell tumour.
- (ii) Fibroid types: innocent (*a*) granulomatous epulis, (*b*) angiomatous epulis, (*c*) fibroid epulis; malignant: fibrosarcomatous epulis.

Consideration will be given now to those tumefactions, be they inflammatory, innocent or malignant neoplasms, which arise from those parts of the mesenchyme which become condensed around the dental ridge downgrowths to form the dental papilla and the periodontal membrane, and which play so intimate a part in the development of the tooth that the tissues in question can legitimately be described as dental mesenchyme.

Tumefactions arising in these tissues may grow into surrounding bone, or form an outgrowth tumour described as a true epulis; and one object of this presentation is the demonstration that every tumour process can appear in either guise.

The tumours in question can be quickly divided into two great groups—namely, the giant-cell and the fibroid tumours. The giant-cell tumour is regarded as having the mononuclear osteoclastic precursor as its cell of origin. This tumefaction is regarded by some pathologists as perhaps an inflammatory hyperplastic process, and by others as a benign tumour. These differences of opinion can be settled only by the pathologist; in the meantime we have to deal with the clinical entities. Further, there is a malignant variety of giant-cell tumour occurring primarily in bones and imitating an osteogenic sarcoma; its metastases may or may not remain true to the primary histological type.

It is convenient to think of the giant-cell tumours of periodontal membrane arising as a hyperplasia representing an excess manifestation of a normal absorptive process —that is, osteoclastic activity.

Why or when a tumour overgrowth starts is not known, but such an overgrowth may be hyperplastic, innocent or malignant, and of either outgrowth or ingrowth type. The fibroid group again may suggest inflammatory hyperplasias, innocent or malignant tumours; one type is found to merge imperceptibly into the other. In the simplest analysis a granuloma is a manifestation of over-repair; the tissue is composed of fibroid and endothelial cells. If one of these tissues is in excess, fibromatous or angiomatous tumours result. In addition a frankly malignant alveolar fibrosarcoma is well recognized.

Let us examine first the ingrowing or central tumefactions of giant-cell and fibroid types.

Giant-cell tumours of the mandible or maxilla always arise in the alveolar bone in the peridental tissues, and thence extend into the body of the bone causing rarefaction, replacement of normal bone by tumour tissue and expansion of cortex. The radiological picture may be characteristic, with fine trabeculæ persisting throughout the tumour.

Geschicter (1949) postulated that the tumour arises from osteoclasts which normally erode the cementum of the milk tooth to allow exfoliation and eruption of its permanent successor. Perhaps many tumours can be so explained, but others arise many years after the milk tooth has been lost. We have seen many such tumours arising in older patients when malocclusion is present. Abnormal lateral pressure on one unsupported tooth causes displacement, and its altered position, according to Professor Amies of Melbourne, is accompanied by bone resorption on one side of its socket and hence local osteoclastic

activity. This mechanism appears to explain a proportion of the late variety of tumour much more satisfactorily than does the theory of Geschicter.

No matter what the radiological appearances, biopsy is necessary for diagnosis, and usually the tumour cavity is curetted and any offending teeth are extracted; but even if the tumour tissue is not removed, a few very small doses of X-ray therapy promote normal repair.

Radiation therapy can be used safely even in children, as the required dose is so small that no growth defects of alveolar bone or teeth due to radiation need be considered.

Three cases confidently diagnosed by competent pathologists as malignant varieties of giant-cell alveolar tumours have been seen. On critical review with Dr. R. Motteram, we have been able to sustain one of these unequivocally. Clinically the tumefactions have formed nodular, easily-bleeding, invasive masses, and some irregular bone absorption has been present beneath.

The other group of fibroid conditions contains, first, the dental granuloma appearing at the tooth apex. This is usually well localized, presenting a characteristic radiological picture; but it is often quite impossible to determine whether the tumour is solid or cystic.

Many an inflammation is not so sharply localized, and a zone of bone absorption may extend outwards, involving the apices of several teeth, or extend into the body of the bone. Histologically the appearances of simple granuloma may be seen; rarely lipoid changes are superimposed. The simple granulomatous condition merges imperceptibly into the histological pattern of a fibroid tissue whose vascularity is small, whose cells are mature and spindle-shaped, and which forms a fine intercellular matrix. This condition is known as *osteitis fibrosa*. As it occurs in the alveolar process, it is a disease distinct from the localized *osteitis fibrosa* of long bones, and has no connexion with von Recklinghausen's disease (Worth, 1937). Rarely its cause is uncertain; in many cases dental sepsis is obvious; in other cases it is only suspected, but sepsis clinical or subclinical seems the most likely ætiological factor. The disease may make its appearance quickly, almost dramatically, when complaint of local discomfort and swelling of but few days' duration may be accompanied by absorption of a zone of subapical bone, perhaps half an inch in diameter. The radiologist cannot make a positive diagnosis at this stage, and exploration yields the characteristic whitish fibroid tissue. The process may remain "localized" with a small area of bone absorption, and may have edges either well limited from surrounding bone, when abscess and cyst may be suspected radiologically, or indefinite edges which allow radiological diagnosis of the condition.

Some process initially destroys bone, and the presence of the fibroid tissue is the first indication of attempted healing of the resorbed bone. In the second stage the fibroid cells commence to lay down bone by direct metaplasia, and granules of bone are formed throughout the tumour; these are slowly enlarged by further deposition on the granule edges until the granuloma becomes densely sclerotic. This second stage is characterized by the radiological appearance of stippling, and the third stage by the sclerosis.

However, the granulomatous process may not remain "localized" as described, but may continue slowly or quickly to advance into adjacent bone, and may spread right through the bone—for example, involving the body and ramus of the mandible—or it may invade and fill the antrum, and characteristically cause ballooning of the alveolar process. This type is referred to as the "spreading" variety while it is localized to one bone; but the disease may over a period of years extend remorselessly throughout the bones of the face and cranium, even to the base of the skull and occipital squama forming the third variety, the "diffuse" type. But even while it is advancing, there is always the attempt at bony healing going on, and it seems never able to catch up with the growing edge of the granuloma.

Treatment of this condition in Melbourne for the past twenty-five years has been by the curetting of small cavities; but recurrence has been not infrequent unless small doses of X-ray therapy are added for a few weeks. This stops further granulation growth, and slowly over a year or so sclerosis of the involved area occurs, with ultimate replacement by normal-looking bone. When deformity of the face or alveolar process has presented, the periosteum has been elevated, the soft vascular fibroid tissue has been cut away to the limits of normal contours, the periosteum is replaced, and subsequently X-ray therapy has been added to prevent continued overgrowth. Radiation has been most effective in causing cessation of growth, stimulation of repair and prevention of recurrences.

Worth (1937) described the three characteristic stages of the disease with regard to the radiological appearances, but gave the impression that the cycle of invasion and subsequent bony healing was not recognized.

A fibrosarcoma commencing in the alveolus forms a characteristic but rare tumour. It may occur on the gingivæ in contact with existing teeth, and the invasive variety erodes adjacent bone and causes expansion of surrounding soft tissues. Destruction of bone leading to pathological fracture in the mandible and widespread invasion of the antrum with ulceration on the alveolar process are later manifestations.

The tumour remains as a well-differentiated fibrosarcoma and does not show bone or cartilage formation, though it may become more dedifferentiated. The onset always in the alveolus, usually in association with teeth, and the absence of osteosarcomatous characteristics, establish a prima-facie case for regarding this neoplasm as a tumour arising from the connective tissues associated with the teeth; one cannot prove that it arises specifically from periodontal membrane. It is certainly a non-osteogenic fibrosarcoma in a category apart from osteogenic sarcoma of the mandible or maxilla.

The line of separation between rapidly growing and invasive *osteitis fibrosa* and osteogenic sarcoma may be very tenuous.

A destructive invasive tumour extending into the maxillary antrum and causing ballooning of the alveolar process was seen in a young aboriginal boy. The amount of destruction made the radiologist diagnose sarcoma, but only on repeated histological examination was the pathologist convinced that the condition was in fact active *osteitis fibrosa* and not osteogenic sarcoma. The tumour was treated with prolonged courses of fractionated X-ray therapy on the basis of the diagnosis of sarcoma. Tumour invasion effects, the gross dental sepsis and the irradiation all contributed to ulceration of the invaded soft tissues. A buccal fistula resulted, which some years later was repaired by plastic surgery.

Diagnosis of these tumours in their early stages is difficult and the appearances may not be characteristic of malignancy, so that the patient comes to the radiotherapist either with a recurrent tumour after initial simple surgical procedures, or because of the receipt of an adverse histological report.

The Epulides.—Epulides have been divided into two groups. First there are those tumours presenting on the alveolar process, originating from other than dental mesenchyme—that is, the group of false epulides. Then there is the group of true epulides arising from the connective tissues closely associated with tooth structures, and on this basis the tumours come within the category of mesenchymal odontomes.

The ingrowth or central types of the giant-cell and fibroid varieties have been described, with innocent and malignant forms of each. It is possible to show exact counterparts of each of these varieties as outgrowth tumours or epulides, thus completing a tidy classification.

Giant-cell epulis is only too common and needs little discussion. It differs from the central tumour only in that it presents as an outgrowth tumour appearing from the gingivus on either side of the alveolar process; maxilla or mandible may be involved, and the tumours may grow to very large size.

The possibility of a malignant variety has been discussed. One would not clinically diagnose a malignant

giant-cell tumour; the diagnosis would be made on the histological findings and would be supported by radiological evidence of subjacent bone destruction with clinical findings in keeping. The giant-cell tumours exemplify the osteoclast or odontoclast and their precursor cells in hyperplastic processes.

The opposite or repair process involves the connective tissue, and both endothelial cells and fibroplasts appear in simple granulation tissue. Granulomatous epulis is one of the commonest manifestations of the over-repair process and is often seen in association with infected teeth, being then a true epulis.

Granulomatous false epulis may occur—for example, in association with osteomyelitis of the mandible; an example of this has been seen. A particularly interesting type of granulomatous epulis is that associated with pregnancy. Hyperæmia of mucous membranes can be induced by œstrin administration, and post-menopausal atrophic rhinitis may be responsive to œstrins. A characteristic angiofibroma develops in the naso-pharynx of sexually undeveloped boys, which is assumed to be associated with a relatively excessive œstrin circulation, and which is responsive to male hormone. The production of the pregnancy epulis is therefore likely to be associated with a hyperæmia of mucous membranes due to the altered hormone balance, particularly if dental sepsis is also a factor.

In any compound tissue in a state of hyperplasia, one element may outgrow the others. The granulomatous epulis is composed equally of fibroid and endothelial cells. However, the vessels may predominate, and all transitions between granulomatous tumours and angiomatous epulides exist. Alternatively, the fibroid cells may predominate and form a fibroid epulis showing just the same histological difference as exists between a root granuloma and central *osteitis fibrosa*. The differences between fibromatous, angiomatous and granulomatous epulides are those of degree only.

It is possible to show further similarity between the fibroid epulis and *osteitis fibrosa*. The latter has been shown to go through a cycle in which healing of the destroyed bone ultimately occurs by metaplastic ossification of the new fibroid tissue. Exactly the same type of ossification can be seen occurring centrally in the larger fibroid epulides, even though marginal growth is being continued. The structural similarities and the behaviour patterns link these two manifestations as one and the same disease process.

Central alveolar fibrosarcoma has its counterpart in an outgrowth tumour—sarcomatous epulis. This tumour may initially be of outgrowth type; but its malignant characteristics are seen clinically by its tendency to rapid recurrence following removal, radiologically by evidence of bone destruction and histologically by a fibrosarcomatous cell pattern.

One of our proven cases occurred in a man who presented with a tumour on the edentulous alveolar margin with considerable bone erosion below. This tumour was controlled with multiple courses of X-ray therapy and remained cured for more than five years.

Conclusion.

Thus all central alveolar tumours of dental mesenchymal origin have their exact counterparts in the true epulides. Two great series exist, the osteoclast and the fibroid; and the transitions between inflammatory hyperplasias and innocent and malignant tumours are impossible to define. But it is possible to follow the pathological processes concerned and classify the tumefactions accordingly, in the realization that not all clinical tumours are neoplasms.

Acknowledgements.

I wish to express my gratitude to Professor A. B. P. Amies, Dean of the School of Dentistry, University of Melbourne, with whom I have had the privilege of working during many years past. Much of the clinical material on which this presentation is based has been examined in association with him, and it has been a great pleasure to carry out the necessary radiation treatment on these patients. Clinical material also has been examined in consultation with Dr. Roy Cash, Dr. Malcolm Piercey and Dr. Vernon Sealey, to whom thanks are due. Dr. R. Motteram has reviewed the sections from the key cases of my collection and has prepared the majority of the photomicrographs for the lantern slides. Professor Amies, Professor E. S. J. King and Dr. J. D. Hicks have kindly made available histological material for review. Dr. H. F. Praagst, Dr. Gwynne Villiers, Dr. Barbara Wood and Dr. Basil Beirman are thanked for their help in making the radiological examinations. Lantern slides have been prepared for me by Mr. C. Young, radiographer in charge at the Austin Hospital; by Miss D. O'Reilley, of the Peter MacCallum Clinic; and by the Visual Aids Department of the University of Melbourne; to all of these my thanks are due.

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TUMOURS OF THE POSTERIOR CRANIAL FOSSA IN CHILDHOOD.

By R. S. HOOPER,

Department of Neurology and Neurosurgery, The Royal Melbourne Hospital, and The Royal Children's Hospital, Melbourne.

ALTHOUGH accurate statistics based upon modern methods of investigation are not available, it is certain that the posterior cranial fossa is one of the common situations for the origin of newgrowths in children. Small (1953) states that tumours of the central nervous system form the largest group of malignant tumours in childhood, these being followed closely by tumours of the sympathetic nervous system. In childhood posterior fossa tumours far outnumber those found elsewhere in the nervous system, more than two-thirds occurring below the tentorium, while in adults the proportion is reversed.

The clinical course of many of these tumours tends to conform to a pattern which was well described by Cushing (1931) in what is now termed "Cushing's composite history".

> A child apparently normal in all respects begins towards the end of the first decade, possibly after a fall or an attack of whooping cough, to have early morning headaches with vomiting. Nothing much is made of this by the family doctor, should he be called in, for the child subsequently feels perfectly well, has had breakfast and wants to go out and play. This daily performance may continue for a considerable time, the child even going to school meanwhile. There may then be a remission of weeks or perhaps months and the episode be forgotten. On their re-occurrence, the symptoms are likely to be more pronounced and are apt to be ascribed to some gastro-intestinal disturbance. This appears to be the more probable since the child finds that straining at stool brings on a headache and there is a tendency to become constipated. What is more, a mild daily laxative usually serves completely to mask the symptoms.
>
> This sort of thing continues off and on until it becomes evident that the child is a little clumsy at play and gets knocked over easily. Very possibly, ere this, the periodic headache will have ceased completely or at least will have occurred at much longer intervals; and

if the parents are observant they may notice that the child's head in the interim has increased more rapidly than it should. This, however, is usually discounted for the child meanwhile has become free from complaints and in all respects appears alert and well.

Matters may run on in this way for an indefinite time, possibly with some increase in clumsiness of movement or in some instances with no noticeable change whatever until it suddenly becomes apparent, perhaps at school, that the child's sight is poor. To counteract this glasses are usually prescribed; but even should an ophthalmoscope be resorted to, a child's retina is less easily examined than that of an adult and, because of the decompressive effects of the enlarging head, the optic papillæ often show no measurable swelling and the fact of their being pale and with margins blurred may easily pass unrecognized.

However, the mode of presentation varies, and the recognition of these variations is important. It is the purpose of this paper to evaluate the clinical features presented by tumours of the posterior cranial fossa in children, and in doing so to refer particularly to diagnosis and prognosis.

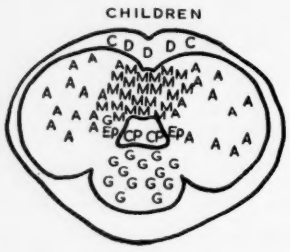

FIGURE I.

Topographical distribution of verified tumours in this series. A = astrocytoma, C = arachnoidal cyst, CP = choroid plexus papilloma, D = dermoid cyst, EP = ependymoma, G = glioma, M = medulloblastoma.

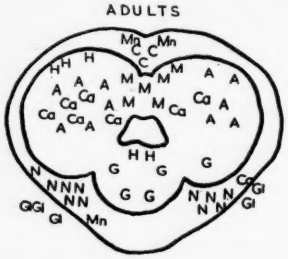

FIGURE II.

Topographical distribution of verified tumours in adults over the same period. Ca = metastatic carcinoma, Gl = *glomus jugulare* tumour, H = hæmangioblastoma, Mn = meningioma, N = neurolemmoma.

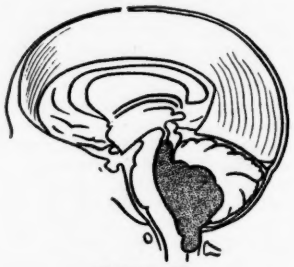

FIGURE III.

Sagittal section of brain illustrating the usual extension of the medulloblastoma arising from the vermis of the cerebellum.

The material upon which this paper is based was obtained from children admitted to the Royal Melbourne Hospital and the Royal Children's Hospital, Melbourne, during the past seven years. Comparison will sometimes be made with a series of adult patients with posterior fossa tumours obtained during the same period. When this series is compared with other published series, such as those of Cuneo and Rand (1952), of Craig, Keith and Kernohan (1949), and of Bodian and Lawson (1953), it is seen that these groups represent a reasonably broad series and illustrate most of the salient features of these lesions.

In many respects the problems presented by children differ considerably from those encountered in adults, and the separation of the material into two groups, one comprising children aged under fifteen years and the other all patients aged fifteen years or over, allows some simplification of what might be a complex problem. Eighty patients were aged under fifteen years, and it is this group, comprising 59·7% of the total, which will provide the subject matter of this paper.

DISTRIBUTION.

In children, the glial tumours of the cerebellum are the dominating group, 83% belonging to this category. In adults the proportion is much smaller, only 27% having a glial origin, because many arise from structures related to the basal cisterns, and the scales are tipped further by the appearance of secondary metastatic tumours in the adult cerebellum.

The anatomical distribution of the lesions also showed a very significant difference, for in children the tumours are most frequently seen involving the mid-line structures—that is, the pons and the vermis of the cerebellum. In the adult group the tumours are distributed over almost all structures and situations in the posterior fossa. These differences are well seen in Figures I and II.

CLASSIFICATION AND FREQUENCY.

The frequency of the various pathological types is set out in Table I.

PATHOLOGY AND CLINICAL MANIFESTATIONS.

Tumours of the Cerebellum.

In childhood, the medulloblastoma and the astrocytoma are the commonest tumours of the cerebellum. Other forms are rare.

The Medulloblastoma.

The development of a medulloblastoma is one of the major tragedies of childhood, for children afflicted with this condition are often bright and intelligent, usually possessing a liberal share of good looks.

Views on the pathology of this tumour are changing. In 1923 Bailey first gave the name to this tumour because he thought that it arose from a cell called the medulloblast, which was said to occur as a stage in the normal histogenesis of medullary epithelium. Although the actual existence of the medulloblast as a stage of development is now considered doubtful, the name remains. Thirty years later, Bodian (1953) endeavoured to clarify the situation by the use of the term "differentiating medulloblastoma". He now groups this tumour with oligodendrogliomata and other unclassified types arising from primitive cells which are capable of differentiation toward either astrocytes or oligodendrocytes.

TABLE I.

Pathological Classification of 80 Tumours of the Posterior Fossa.

Type of Tumour.	Number of Cases.	Percentage.
Gliomata:		
Medulloblastoma	27	34·0
Astrocytoma	23	27·0
Glioblastoma multiforme	2	2·5
Glioma of the brain stem	15	18·8
Ependymoma	3	3·7
Miscellaneous:		
Choroid plexus papilloma	2	2·5
Arachnoidal cysts	2	2·5
Dermoid cysts	3	3·7
Unverified	3	3·7
Total	80	—

The medulloblastoma usually arises in the mid-line, and as it enlarges it invades and destroys the vermis of the cerebellum and the neighbouring portions of the hemispheres. It fills up the fourth ventricle and spills over into the subarachnoid space of the *cisterna magna*. Here it may extend downwards in a long tongue of tissue overlying the cervical portion of the spinal cord, so that occasionally the first clinical manifestations of the tumour

may be due to this downward extension, and the patient presents with all the manifestations of a high cervical spinal cord tumour. Sometimes the tumour spreads round the medulla as a thick collar of tissue or protrudes through the lateral foramina of Luschka to appear in the lateral recess (Figure III).

More widespread dissemination occurs later, and seedling deposits of the tumour may be found over the cerebral hemispheres or down to the lower end of the spinal theca. In Figure IV the situations of these tumours are superimposed. The predisposition for mid-line structure is

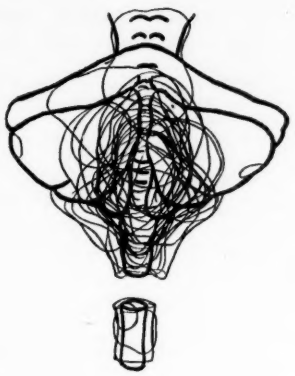

FIGURE IV.
Superimposed traeings of the medulloblastoma in this series.

clearly seen. The sex incidence was equal, although other reported series, notably that reported by Cushing, suggest that there is a strong preponderance of males, especially those aged under five years.

The medulloblastoma has the lowest age incidence of all the tumours of this group (Figure V). In some infants manifestations of the tumour occur so soon after birth that it is obvious that the neoplasm commenced during intrauterine development. The average age at the time of operation was 4·5 years, and the duration of symptoms

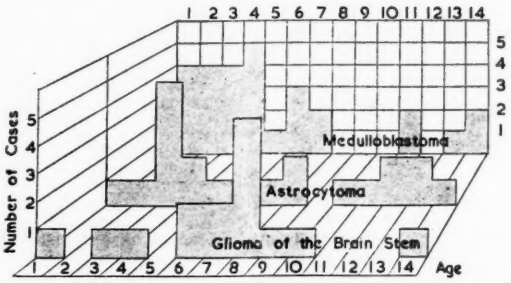

FIGURE V.
Graph showing the age incidence of the three common cerebellar tumours.

before admission to hospital was usually short. Although the average duration was eleven weeks, in the majority of cases the period elapsing before admission to hospital was less than this.

In this series of 27 children, headache, vomiting and ataxia were manifest as symptoms in about the same proportion of cases. It seems probable that headache was more frequent than is indicated here, as many of the children were too young to be able to voice their complaints. In these, vomiting was the prominent manifestation, and some of these children were treated as suffering from gastro-intestinal conditions until obvious enlargement of the head, drowsiness or overt cerebellar signs proclaimed the intracranial ætiology. The time of appearance of these symptoms before operation has been set out in Figure VI.

The ataxia exhibited by this group of patients is of the "trunkal" or vermis type. Initially the gait becomes slightly unsteady or "wobbly", or the child, having learned to walk, retrogresses and later finds it impossible to walk or stand. There is difficulty in sitting up, and in the final stage it is impossible to hold the head up. During this time there may be no trace of incoordination in independent limb movement.

Other manifestations are less frequent, but some require attention:

1. Head tilting has often directed attention to the cervical region and may, at times, induce mild scoliosis, diverting attention away from the origin of the lesion.

2. Apathy, listlessness and personality change may be prominent. The child who normally runs around outside with his friends will be found sitting down indoors with little spontaneous activity. Sometimes the apathy, vomiting and mild neck stiffness suggest tuberculous

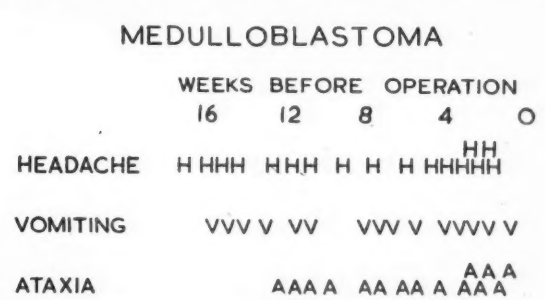

FIGURE VI.
Common manifestations of the medulloblastoma charted according to the time of first appearance. The capital letters indicating symptoms are placed at the time of their occurrence in relation to the time of operation. H, headache; V, vomiting; A, ataxia.

meningitis. Most frequently this problem is resolved by time, but unless investigations are proceeded with at an early stage, the days will slip by, until suddenly all the grave manifestations of the posterior fossa tumour appear with catastrophic suddenness.

3. Pain in the back and legs, followed by paraplegia with sphincter paralysis, is not a frequent mode of onset; but two children presented with the signs and symptoms of a spinal tumour. Cerebellar signs were effectively masked, and headache was absent. The first indication of the tumour was respiratory failure due to direct medullary pressure.

In this group, headache, vomiting and ataxia occurred with almost equal frequency. In the older children, headache and vomiting had been present for more than four months before admission to hospital, but in the infants symptoms were usually of less than three months' duration. Occasionally the tumour was manifest only a few weeks before the child was admitted to hospital for treatment.

The Astrocytoma.

Although it is still regarded as an infiltrating tumour with no distinct line of cleavage between tumour and normal brain tissue, the astrocytoma tends to remain more localized and circumscribed and is not associated with secondary deposits elsewhere in the central nervous system. Tumours of this type may be diffusely invasive or occur as a single circumscribed nodule. Cyst formation is frequent, producing a partly solid and cystic tumour, as in Figure VII, or a simple cyst in which little evidence of neoplastic tissue may be found. Like the medulloblastoma, these tumours tend to originate in the mid-line of the cerebellum; but as growth continues they tend to expand

laterally into either hemisphere rather than to extend into the basal cisterns.

In the diagram (Figure VIII) cystic and solid portions of the astrocytomata in this series are superimposed. The widespread involvement contrasts greatly with the central localization of the medulloblastoma group.

Twenty-two children in this series had tumours histologically verified as astrocytomata; the average age of the patients in this group on their admission to hospital was six and a quarter years (see Figure V), and the duration

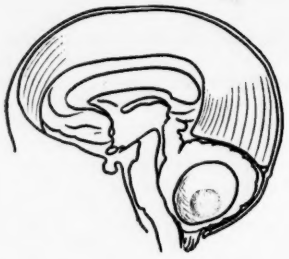

FIGURE VII.

Sagittal section of brain illustrating an astrocytomatous cyst with a mural nodule.

of symptoms before admission to hospital was nineteen and a half weeks—a significant period when compared with that found amongst patients with medulloblastomata. The manifestations are again set out against the time of their appearance in Figure IX. In spite of the long duration of symptoms, or perhaps because of the long and insidious course, a number of children were brought in too late to avert gross loss of visual acuity resulting from the high-grade papillœdema, and two children became quite blind before operation.

The characteristic symptoms correspond with the well-established pattern regarded as typical of cerebellar tumours. The duration of these manifestations was significantly longer than in the medulloblastoma group, as shown in Figure IX. Headache, vomiting and ataxia were the most frequent clinical manifestations. The next most frequent complaint was diplopia; more than half the patients complained of double vision, and four had gross visual loss due to papillœdema. Thus visual disturbance

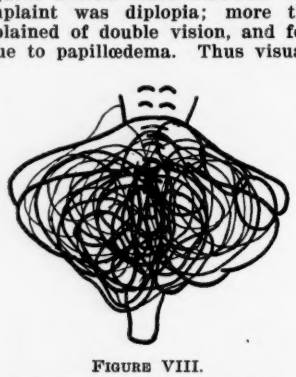

FIGURE VIII.

Superimposed tracings showing the situation of the cerebellar astrocytomata. Heavy lines indicate the site of solid tumour; thin lines represent cysts.

is a prominent manifestation of this tumour, but it is seen at a late stage, usually only two or three weeks before operation. Apathy, listlessness and personality changes were also frequently seen.

The clinical signs produced by these two tumours have similarities and differences. A large head with a cracked pot note on percussion is found in the younger children in each group. In both types papillœdema was usually present on the child's admission to hospital, but gross visual loss, diplopia, squint and nystagmus were seen more commonly in the astrocytoma group. Ataxia was seen in both groups, but in the mid-line medulloblastoma group the defect was mainly in gait and stance, independent limb movement being well coordinated. In the group with more laterally situated astrocytoma, incoordination of limb movement was more pronounced. In both types before operation nystagmus was an inconstant feature.

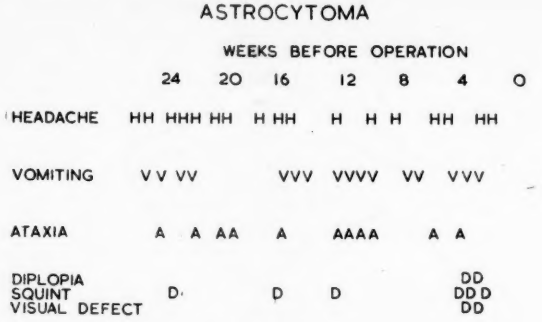

FIGURE IX.

Common manifestations of the cerebellar astrocytoma charted against the time of first appearance. The same convention as in Figure VI is employed. D represents the occurrence of diplopia, squint or significant visual loss.

Tumours of the Brain Stem.

Glioma of the Brain Stem.

Although a pineal tumour may involve the brain stem, this lesion is usually considered to be a supratentorial lesion. The only other condition now commonly encountered in childhood is the glioma of the brain stem, which is a diffusely invasive tumour, often spreading widely through the brain stem before any abnormality is manifest. The

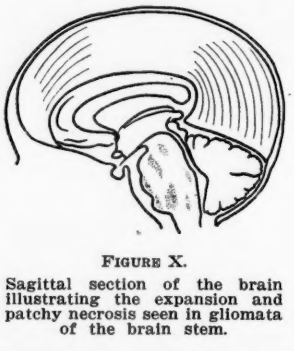

FIGURE X.

Sagittal section of the brain illustrating the expansion and patchy necrosis seen in gliomata of the brain stem.

cells are at first well differentiated and are inextricably mixed with normal tissue, but sooner or later the neoplastic change alters and anaplasia becomes rife. Some of the infiltrated areas undergo rapid expansion, and in these areas masses of abnormal cells rapidly expand beyond the limits of their blood supply (Figure X). Necrosis and hæmorrhage occur, causing a sudden access in symptoms.

Fifteen children of the series belonged to this group. The average age on admission to hospital was six years and the average duration of symptoms was eleven weeks (see Figure V). The common mode of presentation in this group was not with headache, vomiting and ataxia, but with ataxia, diplopia and paralysis of the lower cranial nerves. Headache and vomiting may occur in the later weeks of the fully developed clinical picture, and usually indicate that the expansion of the brain stem is now producing obstruction to the flow of cerebro-spinal fluid. Papillœdema may develop at this stage, but usually the diagnosis is already made by the early recognition of

ataxia, squint and lower cranial nerve palsies in the absence of papillœdema. The time relations of these manifestations are seen in Figure XI.

Tumours of the Fourth Ventricle.

The ependymoma and the choroid plexus papilloma were the only intraventricular tumours encountered. These provide a sharp contrast in their degree of malignancy. The former resembles the medulloblastoma in almost all its clinical features. It is a rapidly growing tumour, which fills up the fourth ventricle, spills over into the basal cisterns, and may give rise to seedling deposits elsewhere. The operative findings and post-operative survival are similar to those accompanying the medulloblastoma.

The choroid plexus papilloma, of which two cases were encountered in this series, is a relatively benign tumour, but it may present with all the dramatic swiftness of a rapidly growing lesion. The clinical picture has no characteristic features, headache, vomiting, ataxia and squint

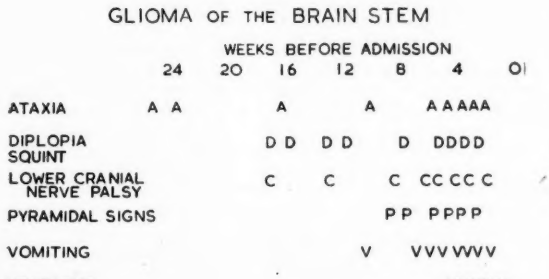

FIGURE XI.

Common manifestations of the glioma of the brain stem set out against the time of first appearance. The additional letters used are: C, cranial nerve palsy; P, pyramidal signs.

being the usual manifestations, and there is no indication of the excellent prognosis which follows early operation. The following case history is of great interest, as it shows that rapidity of onset and gross signs may be associated with small lesions capable of easy removal.

A., aged eleven years, first experienced headache twelve days before admission to hospital. The pain was occipital in situation and was severe and intermittent. Several attacks occurred each day. Three days before the child's admission to hospital, vomiting commenced and there was double vision. Examination of the patient revealed slight neck stiffness, gross bilateral papillœdema, a bilateral sixth nerve palsy and an unsteady gait. Contrast ventriculography with "Myodil" revealed only moderate dilatation of the ventricles, with a small filling defect of the lower portion of the fourth ventricle, causing obstruction to the outflow of contrast medium. At operation a protuberant choroid plexus was seen; this was removed, and the remnants were coagulated with the diathermy. Rapid recovery followed. Examination of sections of the excised plexus revealed the typical structure of a papilloma of the choroid plexus.

Tumours of the Basal Cisterns.

In childhood only two expanding lesions of the basal cisterns are encountered sufficiently frequently to justify discussion.

The arachnoidal cyst is not common and has no pre-operative features which distinguish it from the cerebellar tumour. The cyst is thin-walled and filled with clear cerebro-spinal fluid, which appears to differ in no way from the cerebro-spinal fluid in the normal subarachnoid space. As the cyst enlarges it may dig itself into the cerebellum to appear as a cerebellar cyst; but the distorted folia of the cerebellum can be distinguished, forming the deep wall of the cyst.

Two such cysts are encountered; in both cases the history suggested a rapidly expanding lesion. The following case is an example.

B., aged two years, had complained of earache or headache for four weeks. He then became lethargic and had no appetite. One week before his admission to hospital, vomiting commenced. He was drowsy and irritable. His neck was held stiffly, and examination of the fundi revealed bilateral papillœdema. Radiographic examination of the skull revealed separation of the sutures. At operation a large arachnoidal cyst lying superficial to the right cerebellar hemisphere was removed. Six years later the child is well and pursuing normal activities.

The dermoid cyst is rather more frequent and presents a more varied and, indeed, a fascinating clinical picture. The dermoid cyst of the posterior fossa is a cyst lined with epithelium and containing hair and sebaceous material. It may be connected to the skin in the region by a sinus lined with epithelium, which passes through a small hole in the overlying bone. The presence of this small rounded bone defect in radiographs is suggestive evidence. The cyst often becomes infected and may enlarge rapidly, with the usual effect on intracranial pressure. Often this infection gives rise to attacks of meningitis, of which the origin is not detected until evidence of a posterior fossa lesion is manifest.

The histories of two of these patients may be considered typical of the modes of presentation.

C., aged four years, complained of headache eight weeks before her admission to hospital. Six weeks later she became listless and would no longer run about. Three days before her admission to hospital she became drowsy and vomited frequently. Two hours before her admission she became unconscious. At this time she could be roused only by painful stimuli and would then move all limbs equally. The plantar responses were both extensor in type. Bilateral papillœdema was present. As the child's condition was rapidly deteriorating, a fine drain tube was inserted into the ventricle in the early hours of the morning. Consciousness then began to improve, and a ventriculographic examination was made in the morning. This indicated a posterior fossa tumour, and at operation a large dermoid cyst containing 80 cubic centimetres of pus and sebaceous material amongst much hair was removed. A rapid recovery was followed by normal activities.

A much longer and perhaps more typical history was presented by the following child.

D., aged two years, had had since birth an intermittent discharge from a sinus in the occipital region. For the past year there had been headache and screaming attacks. Later the headache became more severe as the sinus stopped discharging. In the past three months there had been attacks of headache with drowsiness, vomiting and neck stiffness, in which the cerebro-spinal fluid contained up to 800 leucocytes per cubic millimetre. No culture was ever obtained. Examination of the patient revealed a small mid-line sinus in the occipital region from which hair protruded. Radiographic examination revealed a clearly defined, punched-out defect in the bone in this region. At operation a large mid-line dermoid cyst was found. Infection had passed through the cyst wall to form small abscess cavities in the surrounding cerebellum. The child did well for many months, but again developed low-grade meningitis which appeared to clear up; the child then died. At autopsy no recurrence could be found, and little evidence of the recent meningitis. The cause of death was not satisfactorily explained.

In a third child multiple abscess cavities were also present, which had almost completely destroyed the left cerebellar hemisphere; but this child has progressed well and is quite normal in every way.

DIAGNOSIS.

With few exceptions it is impossible to forecast with any certainty what is the nature of the posterior fossa tumour which occurs during childhood. The following brief résumés of histories of varying lesions indicate the impossibility of an adequate pre-operative diagnosis.

E., aged three years, had a three weeks' history of headache, morning vomiting, staggering gait and clumsiness of the hands. Examination of the child revealed papillœdema, ataxia and incoordination of hand movement. The cranial sutures were separated.

F., aged one and a half years, had a four weeks' history of vomiting and ataxia. One week prior to examination a squint developed. Examination of the child revealed papillœdema, bilateral sixth nerve palsy, ataxia, tremor and incoordination of hands, and separation of cranial sutures.

G., aged eleven years, two weeks prior to examination suffered from headache and later vomiting. Two days before the child's admission to hospital diplopia and increasing drowsiness developed. Examination revealed gross papilloedema, bilateral sixth nerve palsy and ataxia.

In these three cases the degree of malignancy of the tumours varied between the large and highly malignant medulloblastoma in the first, the relatively benign cystic astrocytoma in the second, and the very small benign choroid plexus papilloma already described in more detail above.

Although these difficulties occur, it is possible to make some tentative diagnosis beforehand on the basis of probability. Thus the small child, aged under five years, who has a short history of headache, vomiting and ataxia of gait and stance, little incoordination of hand movement, together with papilloedema, and whose skull radiographs do not show sutural separation, is likely to have a medulloblastoma.

An older child, especially if aged over eight years, with a history of headache of more than six months' duration, is more likely to have an astrocytoma, and this is more likely if there are unilateral cerebellar signs.

The child who presents with a short history of ataxia, squint and other cranial nerve palsies, but who fails to complain of headache and in whom papilloedema is absent, is likely to have a brain-stem glioma.

Dermoid cysts are less common; but in some cases the diagnosis can be made with certainty once the condition is suspected and the diagnostic features are sought for.

The initial mode of presentation often leads to an erroneous diagnosis. Some of the smaller children were regarded as presenting feeding problems until the expanding head or increasing drowsiness proclaimed an intracranial lesion. Two infants were thought to have a congenital–non-neoplastic form of hydrocephalus until investigations revealed that the cerebro-spinal fluid obstruction was due to a posterior fossa tumour. In four children the cellular reaction to the tumour suggested a meningeal infection; tuberculous meningitis was suspected when the child presented with a three weeks' history of headache, apathy and squint. As was stated above, two infants with medulloblastomata presented as suffering from spinal tumours.

In nine children the early appearance of a squint confused the initial diagnosis. The strabismus occurred most frequently with the glioma of the brain stem, but sometimes occurred early with the astrocytoma. It did not occur at an early stage in the development of the medulloblastoma. In two children the squint was so far in advance of the other manifestations that an operation was undertaken for its correction before other signs indicated the neoplastic origin of the squint.

Differential Diagnosis.

The various conditions which may be simulated by the posterior fossa tumour in its early stages have already been discussed. There are a number of other conditions which closely simulate the clinical picture of the posterior fossa tumour. In most of these conditions it is the obstruction to the cerebro-spinal fluid flow through the ventricular system which produces the more obvious manifestations, so the similarity may be well understood. Although the similarity in the clinical pictures may be so great that diagnosis is not possible before air studies have been made, there are often some distinguishing features.

The conditions most often confused are all situated in or close to the mid-line structures of the brain. The following are examples.

Stricture of the Aqueduct of Sylvius.

In small infants stricture of the aqueduct of Sylvius presents as one of the causes of infantile hydrocephalus without any specific distinguishing features; but in the older children lassitude and drowsiness followed by ataxia, incoordination and headache may be the presenting symptoms, while examination reveals papilloedema, ataxic gait and often a squint. Superficial examination of the child reveals a large head, with evidence that the posterior fossa is small. Radiographs show more clearly the disparity between the supratentorial and infratentorial spaces. The following clinical history is typical of the manifestation of this condition in children aged over five years.

H., at the age of nine years, became awkward in his movements; his gait became ataxic. Headaches commenced and were associated with morning vomiting. At the same time his school work deteriorated and he became lethargic. Examination of the child revealed papilloedema and a sixth nerve paresis. There was incoordination of hand and finger movements, and his gait was ataxic and slightly spastic. A ventriculogram indicated a stricture of the aqueduct, and the child made a good recovery after a third ventriculostomy. He has continued to enjoy normal activities for seven years.

Occlusion of the Foramina of Magendie and Luschka.

Occlusion of the foramina of Magendie and Luschka, which obstructs the outflow of cerebro-spinal fluid from the fourth ventricle, results in a considerable degree of dilatation of the ventricular system. There are two common forms, as follows:

1. The congenital type. In this the foramen of Magendie is closed by a thin transparent film of arachnoid, which balloons out into the posterior fossa. The cerebellar hemispheres become pushed upwards and the brain stem forwards, so that the greater part of the posterior fossa is occupied by the huge fourth ventricle. This condition at operation looks like a huge cyst with the small cerebellum sitting on top of it, the appearances leading to the erroneous description of a "posterior fossa cyst".

2. The acquired type. This results from posterior basal meningitis, though often enough it is difficult to ascertain when this process began. The arachnoid tissues of the basal cisterns become thickened and infiltrated, forming a complete and formidable barrier to the passage of cerebro-spinal fluid. In this condition ventricular dilatation may be considerable, but never attains the same degree as in the congenital type. Although the condition is of long standing, the development of symptoms may be rapid and may closely resemble that of the posterior fossa tumour, as in the following case.

I., aged eighteen months, had survived a difficult birth and had progressed very well until he began to walk by himself. He then developed attacks of screaming and irritability, and became so ataxic over a period of two or three weeks that he was hardly able to sit up. Papilloedema developed. A ventriculographic examination revealed considerable dilatation of the entire ventricular system. At operation a dense arachnoiditis sealed off the outlet from the fourth ventricle and gummed up all the structures of the basal cisterns.

Other Tumours.

Pineal tumours and gliomata rising in relation to the lateral wall of the third ventricle are uncommon, but closely resemble cerebellar tumours, as they cause ventricular obstruction and may also involve some of the long tracts at the upper end of the brain stem to produce incoordination of movement and ocular palsies.

The more common craniopharyngioma occurring in the suprasellar region may also produce headache, vomiting and papilloedema, and in the absence of other distinguishing features the tentative diagnosis made is usually that of the more common posterior fossa tumour.

Investigations.

Although it is true that in some children a diagnosis can be made with certainty, in the majority no clear-cut diagnosis can be made, and ventriculography is resorted to in almost all cases.

Because complete replacement of the cerebro-spinal fluid in the ventricles is often followed by a considerable upset, attempts have been made in recent years to obtain all the information required without great disturbance of the intracranial pressure. Small amounts of gas injected into the ventricles may be manipulated into the area suspected by positioning of the head, as suggested by Ziedses des Plantes (1950). Heavy contrast material, such as "Myodil"

or "Pantopaque", has also been used, and if the selection of the case is satisfactory striking results can be obtained, as in the child with the papilloma of the choroid plexus.

Any of these methods may reveal filling defects or distortion of the fourth ventricle, as shown in Figure XII; but the characteristic findings in the case of cerebellar tumour at the stage when the patient usually comes to operation is dilatation of the lateral and third ventricles with dilatation of the aqueduct, which is kinked forwards at its lower end and obstructed at this point by the pressure of the posterior fossa tumour (Figure XIII).

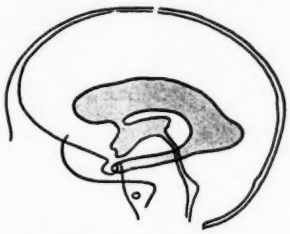

FIGURE XII.

Tracing of ventriculogram of glioma of brain stem (see Figure X) illustrating the backward displacement and distortion of the fourth ventricle.

MANAGEMENT.

Owing to the difficulties in making a certain diagnosis before operation, it is necessary that all children should be subjected to operation and an adequate exposure of the posterior fossa obtained. When the infiltrating tumour is exposed, the microscopic examination of a frozen section will help to determine whether complete removal is to be desired (as in most cases of astrocytoma) or whether, as is often the case with the medulloblastoma, sufficient tumour material should be removed to ensure relief of the

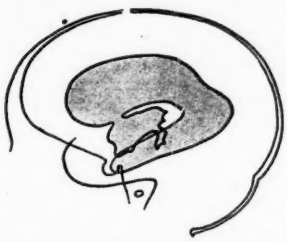

FIGURE XIII.

Tracing of ventriculogram showing the dilatation of lateral and third ventricles and the kinking and obstruction of the aqueduct, common findings in the medulloblastomata and in some astrocytomata (see Figure III for comparison).

cerebro-spinal fluid obstruction, while later attempts to control growth are made by deep X-ray therapy. In almost all cases except those in which the infiltration around the basal cisterns was so gross that removal was hopeless, the aim has been to achieve complete macroscopic removal of the tumour. The one exception to this routine is the patient with a brain-stem glioma, who, after confirmation of the diagnosis by air studies, is subjected to deep X-ray therapy.

RESULTS.

The medulloblastoma has lived up to its reputation as a highly malignant tumour. Only one child has survived for longer than six years. Another child died from other causes four years after operation. Only three others survive, and they were recent additions to this series.

Among the 23 children who developed an astrocytoma, one died before operation, two died in the immediate post-operative period, and two were known to survive more than a year after operation, but have been lost sight of.

The remaining 17 children have survived for periods varying between seven years and three months. All are well, but three who were blind before operation have remained blind.

Of the 15 children with gliomata of the brain stem, only three survive, and these belong to the older age group. Except for the occasional child who developed a cerebro-spinal fluid block and presented with papillœdema, this group was treated by deep X-ray therapy alone. When the tumour caused obstruction, a posterior fossa decompression was carried out and deep X-ray therapy was given soon after. In these few cases neither procedure appeared to achieve much relief.

Of the children with ependymoma of the fourth ventricle, only one survives, while both children with choroid plexus papillomata survive and appear well.

With one exception all the patients with benign cystic tumours have done well.

When these results are summarized, it is at once apparent that the highly malignant tumours which metastasize within the cerebro-spinal fluid pathways — for example, the medulloblastoma and ependymoma — recur almost inevitably, although occasional long-term survivals occur.

With the remaining groups the story is very different. Those who survive operation for an astrocytoma do well and many appear to be completely cured. Some of the diffusely infiltrating astrocytomata may be expected to recur later.

The patients with benign cystic conditions do well, even though other infective complications may sometimes be established.

Of the 80 children in this series there are 31 survivors. In three cases no follow-up has been possible, and it is probable that these children are now dead.

SUMMARY.

Tumours of the posterior fossa may present with variations on the old, well-established syndrome of headache, vomiting, papillœdema, ataxia and incoordination. Some differentiation between the various types may be possible from the age incidence, the duration of symptoms, and the symptoms and signs themselves.

Ventriculography may complete the diagnosis in some cases, but in most operation and microscopic examination of the tumour are necessary. The results justify the early determination of the condition in this manner.

ACKNOWLEDGEMENTS.

Due acknowledgement is made to the members of the staff of the Royal Children's Hospital, Melbourne, who referred most of the patients in this series. Dr. E. Graeme Robertson's help in diagnostic problems, particularly in the use of pneumoencephalography in the brain stem lesions, was invaluable. Dr. R. Kaye Scott and his colleagues at the Peter MacCallum Clinic have controlled the radiotherapy which was used in most of the neoplastic conditions.

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OBSERVATIONS UPON 250 CASES OF BLEEDING PEPTIC ULCER.

By W. K. MANNING, M.R.A.C.P.,
Repatriation General Hospital, Concord, New South Wales.

DESPITE the voluminous literature upon the subject, there is still no general agreement even upon the basic principles to be followed in the management of bleeding peptic ulcer—a common, serious and alarming condition. When principles are propounded they are often platitudinous and offer little assistance in the management of a particular case. These considerations perhaps offer enough justification for yet another contribution to a well-worn theme.

This series of 250 patients comprises all the patients with bleeding peptic ulcer admitted to the Repatriation General Hospital, Concord, over the five-year period from 1947 to 1952. Most of the patients were observed at first hand throughout their illnesses by myself, a physician on the full-time staff of the hospital.

It is proposed to subdivide the material into three main sections: Section I, an analysis of 22 fatal cases; Section II, observations upon the non-fatal cases; Section III, discussion—an attempt to draw some deductions from the study concerning the management of bleeding peptic ulcer.

Section I.

The following is an analysis of the 22 fatal cases.

The Nature of the Dyspeptic History.

Thirteen patients had had ulcer dyspepsia for a number of years, five had had ulcer dyspepsia for several months, and four had only a short history of ulcer symptoms or none at all.

History of Previous Bleeding Episodes.

The history of previous episodes of bleeding is set out in Table I.

TABLE I.

Number of Previous Bleeding Episodes.	Number of Cases.
0	19
1	2
2	0
3	0
4	1
More than 4	0

Nature and Site of Ulcer.

The nature and site of the ulcer as revealed at autopsy were as follows: chronic gastric ulcer, eight cases (all ulcers over two inches in diameter); chronic duodenal ulcer, five cases; acute gastric ulcer, five cases; acute duodenal ulcer (an "erosion"), one case; no autopsy, three cases. In 14 of the 22 cases no definite diagnosis of ulcer had been made prior to the fatal illness.

Ages at Death.

The ages of the patients at death are shown in Table II.

Number of Hæmorrhages during Fatal Illness.

The number of separate brisk hæmorrhages during the fatal illness are shown in Table III.

Causes of Death following Surgical Treatment for Bleeding Ulcer.

Six patients died after surgical treatment to arrest hæmorrhage from an ulcer. One patient died from continued bleeding from an acute ulcer in the cardiac portion of the stomach, after exploration of the stomach through an anterior incision had failed to demonstrate a peptic ulcer. A subphrenic abscess was also found at autopsy.

A second patient died from continued bleeding from two acute ulcers in the cardiac portion of the stomach after partial gastrectomy.

In a third case a gastrectomy was performed. The patient died next day with pulmonary œdema after a transfusion of two litres of blood. At autopsy an ulcer was found at the cardio-œsophageal junction, though no bleeding had occurred since the operation.

In the remaining three cases partial gastrectomy controlled the bleeding, but the patients died of peritonitis from leaking or ruptured suture lines.

TABLE II.

Age (Years).	Number of Cases.
Under 40	3
40 to 50	2
50 to 60	7
60 to 70	6
Over 70	4

Other Serious Associated Diseases.

In 11 cases other serious diseases were present and contributed materially to the death from bleeding ulcer.

In one case there were bilateral bronchiectasis and pulmonary fibrosis with considerable reduction in vital capacity.

In a second case there was hypertension with left ventricular hypertrophy and recurrent episodes of left ventricular failure. Active pulmonary tuberculosis was also present.

TABLE III.

Number of Hæmorrhages.	Number of Cases.
1	7
2	1
3	5
More than 3	2
Intermittent or continuous over a long period[1]	3

[1] In four cases, death was due to complications following successful operation to arrest the hæmorrhage.

A third patient suffered from active tuberculous disease of the spine, and a recent diagnosis of Korsakoff's psychosis had been made.

Coronary atherosclerosis and ventricular fibrillation were present in the fourth case. The patient was aged thirty-four years, and the hæmoglobin value was five grammes *per centum* at the time of sudden death. Autopsy revealed acute duodenal erosion and considerable narrowing of the left coronary artery, but no recent bleeding.

In the fifth case a perigastric abscess followed a perforation four months previously, and was drained just prior to the patient's death.

The sixth patient had *polycythæmia vera* with splenomegaly and considerable general physical debility.

The seventh patient suffered from advanced emphysema and chronic bronchitis, with dyspnœa on slightest exertion.

In the eighth case aortic stenosis and left ventricular hypertrophy of marked degree were present.

The ninth patient had essential hypertension, with a blood pressure of 250 millimetres of mercury, systolic, and 150 millimetres, diastolic. An episode of cerebral thrombosis had previously occurred.

The tenth patient was aged sixty-nine years, and suffered from advanced emphysema and chronic bronchitis; his physical state was feeble.

In addition there were five cases in which acute pulmonary œdema was found at autopsy. This may have been

due partly or wholly to over-energetic blood transfusion; in the following case at least, death was almost certainly due to this cause.

A patient, aged thirty-eight years, was admitted to hospital on December 22, 1947, with a history of melæna and a hæmoglobin value of 6·9 grammes *per centum*. At 9.15 p.m. hæmatemesis occurred. A blood transfusion was begun and his condition became quite satisfactory. Between 9.15 p.m. and 3 a.m. he received intravenously two litres of blood and three litres of serum. At 3 a.m. he was noted to be in respiratory distress and cyanotic, and examination revealed clinical signs of pulmonary œdema. He died in a short time, and autopsy disclosed acute pulmonary œdema, an active duodenal ulcer with clot in the base, but no blood in the bowel.

Section II.

The following observations are presented on 228 non-fatal cases of bleeding ulcer treated medically.

About 20% of the cases were classified as mild; that is, after the bleeding had stopped the patients had a hæmoglobin value of nine grammes *per centum* or more. Approximately 75% of patients had only one hæmorrhagic incident, usually occurring prior to their admission to hospital. About 25% (54 patients) had recurrent severe bleeding; 14 of these had two separate hæmorrhages, 26 had three, four or five separate hæmorrhages, and 14 had between five and 10 separate hæmorrhages.

Assessment of the Progress and Extent of Bleeding.

Great difficulty was experienced in determining whether bleeding was continuing or not, and also in assessing the severity of the bleeding, because of the following observations:

1. Vomiting of blood or its passage *per rectum* may be delayed many hours after the actual occurrence of free bleeding. In one case the interval was seven hours; in another (to refer back to one of the fatal cases) the interval was forty-eight hours, and no blood was actually seen until ten minutes prior to death, though the occurrence of severe bleeding had been established clinically for forty-eight hours and the patient had received a transfusion of three litres of blood. Autopsy showed the stomach and bowel to be full of blood.

2. The signs of shock were not found to be reliable criteria of the extent of blood loss. Nausea induced by a small amount of blood in the stomach may produce all the signs of severe shock; these signs may then disappear rapidly when the stomach is emptied by vomiting. Moreover, simple anæmia, even of severe degree, did not produce the signs of shock in a patient lying comfortably in bed. Patients with a hæmoglobin value even as low as three or four grammes *per centum*, in bed several hours after a severe hæmorrhage, usually showed no signs of shock apart from tachycardia; the blood pressure in these patients is usually found to be within normal limits.

3. Measuring the amount of blood vomited was not found to be a reliable criterion of blood loss, since considerable dilution by stomach juice can occur without this fact being obvious even on inspection. Hæmoglobin values estimated several days after all bleeding had ceased frequently showed that the measured amounts of "blood" vomited must have contained a considerable proportion of fluid other than blood.

On the whole, the frequent estimation of the hæmoglobin value was found to be the most reliable indication of the extent of blood loss, despite the theoretical objections to its accuracy.

Differential Diagnosis.

Experience in this series of cases indicated that any free bleeding from the upper part of the gastro-intestinal tract should be regarded as due to peptic ulcer unless there is good evidence for an alternative diagnosis.

Normal findings on barium meal studies (frequently multiple), normal gastroscopic findings and atypical histories were often followed closely by the occurrence of bleeding from a peptic ulcer; many patients in this series were radiologically examined within seven days after hæmorrhage from what subsequent events indicated to be a peptic ulcer, but no ulcer could be found. The explanation of this state of affairs is probably twofold: firstly, there is a high degree of inaccuracy in the diagnosis of peptic ulcer by any means; secondly, as is confirmed by the autopsy findings, the incidence of severe bleeding from acute, shallow, transitory ulcers is quite high.

For practical purposes the only other conditions causing bleeding from the upper part of the gastro-intestinal tract are, of course, cirrhosis of the liver and carcinoma of the stomach. During the period of this study there were 14 fatal cases of hæmatemesis due to cirrhosis of the liver, one case due to carcinoma of the stomach and one due to carcinoma of the second part of the duodenum.

In regard to the diagnosis of cirrhosis of the liver, it was noted that serious hæmatemesis usually occurred late in the course of this disease and indeed frequently precipitated death from "liver failure". It was noted that the patient who had hæmorrhage from œsophageal varices was nearly always in much worse physical shape than the patient who had hæmorrhage from an ulcer, and was obviously suffering from some serious systemic disorder in addition to the blood loss; he was usually drowsy or comatose, had a hard liver which might or might not be palpable, often showed a mild degree of jaundice and frequently had spider nævi, ascites, or a hard, palpable spleen. The differential diagnosis seldom presented any real difficulty.

Carcinoma of the stomach was found to be an infrequent cause of severe and repeated bleeding from the gastro-intestinal tract; but bleeding from this lesion is usually impossible to distinguish from that due to simple ulcer. However, the rarity of severe bleeding from carcinoma renders the differential diagnosis comparatively unimportant.

Section III.

A certain proportion of patients with bleeding peptic ulcer will fail to respond to any form of medical treatment and will die unless the bleeding vessel is tied off. The burning question of how these patients can be recognized prior to death and submitted to timely operation still remains unanswered.

Various simple-sounding formulæ have been propounded, but none of these have been found to stand up satisfactorily to the test of experience.

It is instructive to apply some of these formulæ to the present series of cases in retrospect, and to note the result.

Perhaps the commonest criterion used to determine the use of surgical treatment is that of recurrent bleeding. Some doctors hold that a single recurrence of brisk bleeding in a man aged over forty years is an indication for surgical treatment; some hold that two or even three or more recurrences are necessary to provide this indication. How does this criterion of recurrent bleeding work out in relation to the present series? Reference to Table III shows that more than one-third of the fatalities from uncontrolled bleeding occurred during the initial hæmorrhagic episode. Reference to the figures again shows that 25% of all patients with bleeding ulcer had one or more recurrences after the initial hæmorrhage; thus in this series 25% of all patients would have to be submitted to operation if one adhered to the criterion of one recurrence as an indication for operation, and even then, one-third of the fatalities (deaths in the initial bleeding episode) would be unaffected by the procedure.

Should one regard two or three or more recurrences of brisk bleeding as an indication for operation? The figures in this series, while indicating that the mortality in cases of recurrent bleeding is considerably greater than in cases of a single hæmorrhage, do not show any strong correlation between the number of recurrent hæmorrhages and the likelihood of a fatal outcome. There is often in addition the practical difficulty, previously stressed, of determining with certainty when bleeding is recurring; and in many cases there is between hæmorrhages insufficient time or improvement in the patient's condition to give him a reasonable chance of surviving a major surgical procedure.

Furthermore, the figures for the non-fatal cases show that a large number of patients had frequent recurrences of severe bleeding, even over periods of several weeks, and yet made satisfactory recoveries without operation.

So much for the criterion of recurrent bleeding; another criterion which has been much advocated for determining when surgical treatment should be employed is that of age. Various studies have indicated that the mortality from bleeding ulcer increases with age. This fact is borne out by the present study, and it would be surprising if it were not so, since it is axiomatic that mortality from any kind of serious trauma increases with age; the mortality from serious surgical trauma such as the operation of gastrectomy likewise increases with age. In other words, the mortality from bleeding ulcer is likely to be much higher in the older age groups whatever form of treatment is employed.

This point is well illustrated by the following case.

A feeble, emphysematous old man, aged sixty-nine years, died eleven days after the last hæmorrhage from a chronic gastric ulcer when his hæmoglobin value was 6·3 grammes *per centum*. Autopsy revealed no evidence of recent bleeding and no other cause of his sudden death. He apparently died because his senile tissues could not survive, even at rest in bed, a degree of anæmia which would scarcely have embarrassed a younger man at rest in bed.

It would seem, then, that no useful criteria can be inferred from this study which would enable one to decide the probability in any given case of whether bleeding would or would not stop without surgical intervention.

The difficulty of deciding in any particular case whether and when bleeding will stop is in no way made easier by wise talk at the bedside. Personal opinions in this situation can be no more than wild guesses unless they are backed up by reliable statistical evidence.

If the statistical evidence does not supply a reliable set of criteria for deciding in any given case whether bleeding is or is not likely to stop without operation (and this would seem to be the present situation), then there are only two alternative procedures—(*a*) to operate on all patients with bleeding ulcer, and (*b*) to operate on none and to accept an inevitable mortality rate.

Few would advocate the first course, as the over-all mortality would thereby be increased rather than decreased, and in addition, many patients with bleeding ulcer do not require gastrectomy as a long-range treatment.

What of the alternative of not operating at all? How serious is the mortality rate in cases of bleeding ulcer treated exclusively by medical means? Figures vary greatly, but it is suggested that the disease is not nearly so lethal as is indicated by some of the figures. Bare percentages do not necessarily tell the whole story. Reference to the case histories in this study dealing with the incidence of other serious diseases in fatal cases of bleeding ulcer will show that, in many cases in which death was attributed to bleeding ulcer, the bleeding ulcer was only one factor, and sometimes not the most important factor, in the patient's death.

It is probable that such considerations apply generally to statistics regarding mortality from bleeding ulcer. Moreover, the death from bleeding ulcer of a senile individual, aged seventy-five years, with serious impairment of his vital functions, is clearly a different matter from the similar death of a vigorous man aged fifty years; yet bare mortality figures take no account of such differences.

Analysis of the mortality figures in the present study along these lines is interesting. Almost all the 250 patients in this series were treated non-surgically; nearly all of the small number of patients who were treated surgically appear in the list of fatal cases. Of the 250 patients, 22 died; six of these died after surgical treatment; of the remaining 16 patients, only four were free of some other severe complicating disease (for details of these diseases see Section I), and the ages of these four men were respectively sixty-nine, sixty-eight, sixty-five and fifty years.

It can, therefore, be stated that of approximately 250 patients treated by medical means, only four died who were otherwise in reasonably good health.

Thus, in this series, the significant mortality of bleeding ulcer under medical treatment is very low, although the mortality from a strictly statistical angle is in the region of 7%.

In the light of all the observations made in this study, it seems reasonable to conclude that in the present state of knowledge the best way to deal with the problem of bleeding peptic ulcer is to treat all patient non-surgically, and to accept an inevitable mortality, which should be reasonably low if the medical treatment is good.

Here again opinions differ on what constitutes good medical treatment. As a result of experience in this series of patients and in a similar number of patients treated since, I am convinced that the one all-important principle to be observed is that of restraint in the transfusion of blood. While no statistical proof can be advanced, it has seemed beyond doubt that free transfusion tended to cause recurrence of bleeding, and it seemed very likely that a number of deaths in this series were contributed to, or caused by, œdema of the lungs brought about by free transfusion. If it is true that free transfusion predisposes the patient to recurrent bleeding, it may do so by releasing peripheral vasoconstriction. Observation does not suggest that variations in the blood pressure as measured in the brachial artery are a significant factor. It is also beyond doubt that mental and physical relaxation is interfered with by the atmosphere of drama and the physical discomfort associated with blood transfusion; this could be an important factor in the recurrence of bleeding. Dilution by the transfused blood of clotting elements such as thromboplastin produced at the site of tissue injury is another possible factor.

The principles of treatment which seemed to bring most success in this series were as follows:

1. A hæmoglobin estimation and provision of suitable blood for transfusion were carried out as soon as possible.

2. No transfusion was given, irrespective of the hæmoglobin value, unless the patient showed persisting signs of shock (not merely tachycardia) after being put to bed, or unless there was recurrence of significant bleeding in a patient whose hæmoglobin value was already in the region of four or five grammes *per centum*.

3. If a transfusion was given, the minimum amount of blood necessary to alleviate circulatory distress was administered.

4. Feeding of the patient with small frequent feeds of egg-flip was begun as soon as nausea had disappeared.

The application of these principles of treatment requires the constant supervision of a physician with considerable experience of bleeding ulcer; the urge to "do something active" almost always leads the inexperienced medical attendant to transfuse the patient too freely, particularly in the presence of recurrent bleeding.

Summary.

The clinical details of 250 cases of bleeding peptic ulcer were closely observed and recorded by one observer.

Analysis of this material fails to provide any reliable criteria by which the small group of patients who will be cured only by surgical means can be selected.

It is suggested that in the absence of such criteria the best results can be obtained by treating all patients with bleeding ulcer non-surgically, and accepting a certain mortality, which is probably not unduly high with appropriate medical treatment.

It is probable that there is a certain inevitable mortality rate among patients with bleeding peptic ulcer who are senile or have some other serious disease, and who are unable to sustain the trauma either of severe blood loss or of operation.

Observation in this series seems to indicate that the most important principle in successful medical treatment may be to restrict the use of blood transfusion as much as

possible; it is suggested that in many cases recurrence of bleeding and/or death from pulmonary œdema result from the free transfusion of blood.

The impressions gathered by the observer in this series of cases have been strengthened by the observation of approximately another 250 cases in the years following the present study.

Acknowledgement.

My thanks are due to the Chairman of the Repatriation Commission for permission to publish this article.

MISSED OPPORTUNITIES IN THE POST-MORTEM ROOM.

By R. F. BUTTERWORTH,
Blackburn, Victoria.

THE overcrowding of medical schools has brought excessive pressure on teaching and research facilities; so that individual cultivation of powers of observation and manœuvre becomes increasingly difficult. Impressions formed during a close association with three teaching hospital post-mortem rooms suggest that a better use of the dead subject might help remedy this situation.

A considerable amount of experimental cardiac surgery was recently carried out on cadavers. The spontaneous interest and offers of help from students were surprising; some very ingenious suggestions were made. Many students stated that they had never before seen the heart and great vessels *in situ* in the fresh subject. They expressed regret that no such demonstrations were given in pre-clinical departments.

The poor equipment for and slipshod conduct of the average post-mortem examination were very noticeable. No attempt was made to interest students or junior practitioners in possible research projects.

The routine autopsy seemed to have become so much a part of the hospital scene that its crudeness and waste were accepted without question. Reform is necessary.

Defective Equipment.

Most post-mortem rooms are structurally adequate, but the lack of easily available equipment shows how far this branch of morbid anatomy has fallen behind. The following three things are essential: (i) An X-ray viewing box to coordinate the appearance of films with autopsy findings, sometimes but not always provided. (ii) A supply of properly sharpened instruments for dissection and operative surgery. Cast-offs from the operating theatre are satisfactory, but the usual massive ebony-handled tools resembling the kit of an eighteenth century naval surgeon are quite unsuitable. Their very look engenders haste and carelessness. (iii) A sucker. No surgeon would operate without one; but suckers are not provided. Instead pathologists are content year after year to hack and grab at organs in a welter of blood-stained fluid, and there is the disgusting spectacle of body cavities being baled out with tins or even mopped up with sponges which are subsequently wrung out over the slab. An efficient water-main type sucker can be purchased very cheaply.

Defective Procedure.

The increasingly common habit of employing an attendant to rip out the organs for subsequent demonstration by the pathologist is bad. Without careful dissection vital facts will be missed.

Thus an experimental right-sided thoracotomy, on a patient who had died three days after the suture of a perforated peptic ulcer, showed enormously distended *venæ cavæ*, dilatation of the right side of the heart, and gross œdema of the lungs. The thoracotomy wound was sutured. An attendant subsequently employed the usual crude method of evisceration, leaving the organs to drain on the slab. When the pathologist arrived half an hour later, the engorgement was no longer obvious and the case was shown as death due to bronchopneumonia. Discreet inquiries revealed that the patient had received four litres of normal saline daily since the operation. A proper dissection demonstration integrated with the clinical history might have caused embarrassment, but would have been an unforgettable lesson of the dangers of reckless intravenous administration of fluids.

Suggested Remedies.

Deficiencies of equipment are easily remedied. To secure sufficient time for the proper utilization of the subject presents more difficulty. Nevertheless some hospitals manage to have cadavers ready by 9.30 a.m., thus leaving ample time before the noon demonstration. Relatives' consent can usually be obtained the night before. The matter must be arranged to suit the medical school, not the whims of porters and undertakers.

Instead of being mere spectators, students should take an active part. Working in groups of three or four, under the direct supervision of the registrar concerned, they would carry out a careful exposure of the viscera, paying particular attention to the presence of fluids, displacement or distension of organs, adhesions *et cetera*. Organs could be palpated *in situ*, but not otherwise disturbed before the arrival of the pathologist. Opportunity might be taken for a review of the gross anatomy.

Pre-clinical students might well be invited to these sessions. Their academic knowledge of anatomy is always stimulating. It would be a useful method of associating the two groups.

After completion of the post-mortem examination the group would attempt to correlate pathological and clinical findings, discussion and questioning being encouraged. In suitable cases a review of the radiological findings would be instructive. It appears that only a small minority of radiologists pay regular visits to the autopsy room.

Research.

The ingenious student should be encouraged to suggest suitable research projects, and every facility given for original investigation. It should be emphasized how little is really known about many common pathological conditions, and how even surgical anatomy is by no means a fully worked out field. The reorientation of the anatomy of the bronchial tree (Brock, 1946) is an example of this. Again the extension of surgical technique is bringing into use many facts which were previously of purely theoretical interest. Thus the variations in the distribution of the bronchial arteries are now important, but are not yet fully determined.

The lymph drainage of tumours has always been a subject of intense interest, but their vascular pattern has been comparatively neglected. Further study, by the use of differential injection techniques *in situ*, is called for.

A bronchial carcinoma derives its blood supply from the bronchial and not the pulmonary arteries (Wright, 1938). Recent work on the venous drainage of the prostate gland has done something to explain the frequent occurrence of vertebral metastases in carcinoma of that organ (Franks, 1953). Studies of the blood supply of other common tumours might yield worthwhile information. Projects of this sort are not beyond the capacity of students under supervision. Even if no fundamental advances are made, something will be learnt of the necessity for patience and accuracy, and of the many pitfalls and disappointments of original research.

Training in Operative Surgery.

Facilities for operative surgery on the cadaver have usually been obtainable by the keen post-graduate. However, every student should be compelled to practise certain essential techniques on the cadaver—for example, *paracentesis abdominis* and *paracentesis thoracis*, cutting down on a collapsed vein, and the extraction of teeth. The modern undergraduate seldom has a chance to carry out such procedures under supervision. The statement that they can be learnt after graduation shows a wicked levity. Anyone who has witnessed a doctor attempting to extract a tooth for the first time on board ship will require no

further persuasion that half an hour's instruction on the cadaver is essential. Unfortunately it tends to be the least competent student who has to take his junior appointment in an outlying hospital and attempt these things for the first time without supervision.

Summary.

1. A plea is made for the fuller utilization of the dead subject in medical schools.

2. Instances of poor equipment and defective procedure in teaching hospital post-mortem rooms are given and reforms are advocated.

3. Some suggestions are made for research projects and training in technical procedures.

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RADIATION DOSES TO THE GONADS IN DIAGNOSTIC RADIOLOGY AND THEIR RELATION TO THE LONG-TERM GENETIC HAZARD.[1]

By J. H. MARTIN, B.Sc., Ph.D., F.Inst.P.,
Physics Department, Peter MacCallum Clinic, Melbourne.

THE extensive work carried out on radiation-induced mutations in animals has indicated that radiation results merely in a speeding-up of the spontaneous mutation rate, and not in the production of anything qualitatively different. It is usually agreed that an increase in the mutation rate must be considered undesirable for most species, and it is probably especially undesirable for man, since the selection pressure against the persistence of detrimental genes is, if anything, reduced in civilized societies, the concept of the "welfare State" being an expression of the principle that civilized society assists its less fortunate fellows. At the present stage of our knowledge, therefore, we can expect that radiation reaching the gonads will increase the frequency of all the distressing hereditary conditions apparent in man. A number of workers have drawn attention to the existence of this danger (Catcheside, 1947 and 1948; Howard, 1952; Mather, 1952; Muller, 1951, 1954*a*, 1954*b*; and Stanford *et alii*, 1952). The danger is growing, as an ever-increasing proportion of the population is being exposed to radiation, both occupationally and in medical diagnosis, and we must consider what acceleration of the mutation rate, in reference to the spontaneous mutation rate, is being produced by this radiation contribution to the population as a whole. It is the purpose of this paper to assess the radiation contribution to the gene material of the population, due to diagnostic X-ray examinations in relation to other sources of radiation.

Methods of Estimating Doses Received by Gonads.

The radiation dose to the gonads has been determined for a wide range of diagnostic X-ray examinations. When possible the doses were measured directly on the patient, in the case of males the dose being determined by the placing of an ionization chamber in contact with the scrotum. In such female patients as it was possible, the dose was measured with an ionization chamber in the posterior fornix, this being assumed to give the dose to the ovaries. In the majority of cases this was not possible, and the dose at the ovaries was assessed by placing an ionization chamber on the skin surface nearest the tube and directly above the ovaries. In such examinations as included the ovaries in the field of irradiation, the dose at the ovaries was estimated from depth dose data. When the field of irradiation did not include the ovaries, the dose was assessed from measurements of the radiation scattered outside the edge of the field. These latter measurements were carried out by the use of a suitable tissue-equivalent phantom, the radiation dose outside the edge of the field being measured at a variety of depths for a number of different conditions of field size and kilovoltage. An example of the results is shown in Figure I. From such curves it is possible, if the distance of the ovaries from the edge of the X-ray beam is known, to estimate the dose they receive.

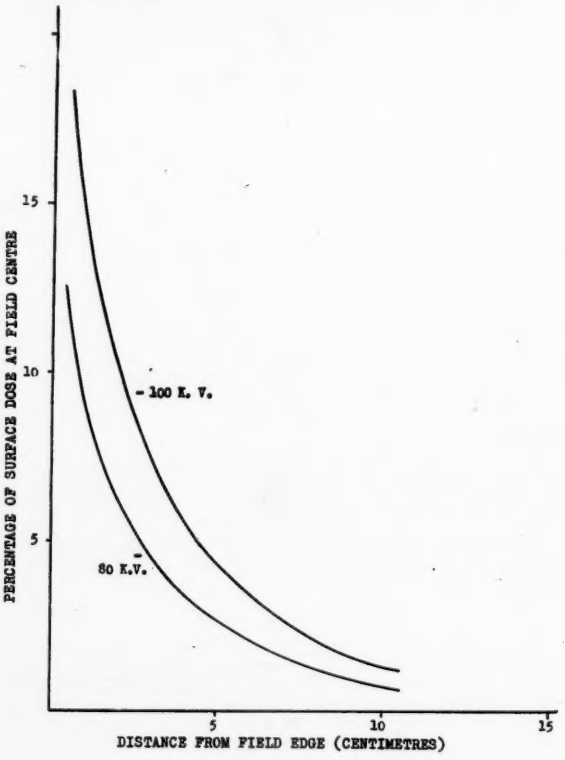

FIGURE I.

Variation for a field size of 20 by 20 centimetres and at a depth in tissue of five centimetres of radiation scattered outside the field with distance from the field edge.

Diagnostic X-ray techniques, of course, vary considerably, and in order to assess the likely range of gonad doses received in any examination, the data obtained by measurement as indicated above have been extended by the use of data from the literature (Ardran and Crooks, 1952; Handloser and Love, 1951; Jamieson, 1952; Kolbow, 1940; Martin and Williams, 1946; Martin, 1947; Neef, 1934; Osborn, 1951 and 1952; Ritter *et alii*, 1952; Stanford, 1951; Stanford and Hills, 1950; Stanford *et alii*, 1952; Sonnenblick *et alii*, 1951; Trout *et alii*, 1952; Weens *et alii*, 1954; Witte, 1933; Zimmer, 1935). By the use of the information provided by Martin (1947) and by Trout *et alii* (1952), the skin and gonad doses received have been estimated. The range of doses found was wide, and the measured and calculated values were in sufficiently good agreement not to differentiate between the two results. Some of the figures obtained are shown in Table I, in which are given the dose range likely with each type of examination, the mean dose for each examination, and the lower doses which result from the use of higher kilovoltages and/or heavy filtration of the X-ray beam.

[1] Read at the annual meeting of the College of Radiologists of Australasia, November, 1954, and accepted for publication May 10, 1955.

TABLE I.
Dose per Film to Gonads.

Type or Site of Examination.	Range (Milliröntgens).		Mean Value (Milliröntgens).		Value when High Kilovoltage and/or Heavy Filtration are Used (Milliröntgens).	
	Testes.	Ovaries.	Testes.	Ovaries.	Testes.	Ovaries.
Skull *et cetera*	0·036 to 0·96	0·013 to 0·4	0·06	0·3	—	—
Chest	0·07 to 1·6	0·3 to 8·9	0·3	2	—	0·12 to 0·6
Pelvis:						
Antero-posterior	140 to 2600	50 to 700	600	300	—	20 to 170
Lateral	—	1400 to 1700	—	1600	—	220 to 1500
Pregnancy	—	180 to 3500	—	1500	—	30
Pregnancy	400 to 6000 (Fœtal gonads)	—	—	—	—	—
Pregnancy	2000 to 30,000 (Male gonads, (vertex presentation)	—	—	—	—	—
Gastro-intestinal tract	—	10 to 1100	—	150	—	—
Lumbar part of spine:						
Antero-posterior	4 to 9·5	20 to 160	5	50	—	7·6 to 13
Lateral	20 to 36	60 to 300	28	150	—	20
Lumbar part of spine—sacro-iliac region:						
Postero-anterior	—	84 to 152	—	90	—	—
Lateral	30	300 to 4100	30	500	—	—
Gall-bladder	—	20 to 60	—	50	—	—
Gall-bladder—cholecystography	3	50 to 160	3	90	—	—
Kidney	2 to 5	6 to 100	2·5	30	—	—
Bladder	—	150	—	—	—	—
Excretion pyelography	100 to 300	32 to 500	140	250	—	—
Salpingography	—	2500 (total)	—	—	—	—
Pædiatrics	—	0·9 to 16·5 *r* per minute	—	—	—	—

Analysis of Data.

Once the doses received at the gonads in various diagnostic examinations have been determined, it is necessary to have a knowledge of the extent and type of diagnostic X-ray examinations being carried out. With some justification, it is assumed that, before passing the age at which reproduction is likely, every person, male and female, undergoes a diagnostic X-ray examination other than in mass radiography. With this in mind, an analysis of the number and type of X-ray examinations carried out at a large general hospital in Australia has been obtained, and this has been taken as representing an average distribution for the country.

Tables II and III show the sites examined and the dose received by the gonads for each examination. It will be seen that as far as males are concerned, about one-third of the total dose is received during examination of the stomach; this accounts for only 8·3% of the total number of people concerned. This type of examination, together with examination of the pelvis and hips, accounts for over 70% of the dose received, representing only some 14% of the cases. The mean gonad dose per examination is 123 milliröntgens.

For females the mean gonad dose is 227 milliröntgens per examination, some 50% of this coming from three types of examinations representing only 6% of the cases. For both sexes the number of chest examinations is large, but they give rise to a very small proportion of the gonad dose. This is due to the low dosage involved in chest work, whether full-size film or mass-miniature techniques are used, even though, in the case of the female, the lower edge of the irradiated region may come quite close to the ovaries.

In addition to the figures listed in the tables, contributions must be added for the doses due to fluoroscopic examination, the dose to the fœtus during pelvimetry and

TABLE II.
Female Subjects.[1]

Type or Site of Examination.	Cases in One Year		Average Number of Films per Examination.	Gonad Dose per Examination (Milliröntgens).	Gonad Dose per Year.	
	Number.	Percentage.			Röntgens.	Percentage of Total.
Extremities	1312	17·5	2·1	1	1·3	0·08
Skull *et cetera*	932	12·4	3·3	1	0·9	0·06
Chest	2184	29·1	1·2	2·4	5·3	0·31
Pelvis	208	2·8	1·6	800	166·6	9·7
Cervical vertebræ	124	1·7	2·3	1·2	0·1	0·01
Hips	240	3·2	2·2	440	105·5	6·2
Shoulders	108	1·5	1·7	3·4	0·4	0·03
Salpingography	16	0·2	3·3	25,000	400	23·4
Urinary tract	368	4·9	2·9	203	74·6	4·4
Cholecystography	344	4·6	4·2	378	130	7·6
Lumbo-sacral joint	256	3·4	4·1	1025	262	15·3
Stomach	416	5·4	2·4	360	150	8·8
Intestinal tract (barium enema)	180	2·4	3·0	520	93·5	5·5
Excretion pyelography	172	2·3	3·9	1360	234	13·7
Ribs	56	0·8	1·9	3·8	0·2	0·01
Dorsal vertebræ	156	2·1	2·1	124	19·3	1·1
Gall-bladder area	348	4·6	1·4	70	24·4	1·4
Retrograde pyelography	36	0·5	3·7	800	28·8	1·7
Bladder	20	0·3	1·4	210	4·2	0·2
Kidneys	12	0·2	2·0	60	0·7	0·4
Liver	8	0·1	1·0	20	0·2	0·1
Total	7496	—	—	—	1702	—

[1] Average dose per examination, 227 milliröntgens.

TABLE III.
Male Subjects.[1]

Type or Site of Examination.	Cases in One Year.		Average Number of Films per Examination.	Gonad Dose per Examination (Milliröntgens).	Gonad Dose per Year.	
	Number.	Percentage.			Röntgens.	Percentage of Total.
Extremities	2256	26·8	2·1	2·1	4·7	0·5
Skull *et cetera*	1052	12·6	3·4	0·2	0·2	0·02
Chest	1740	20·8	1·3	0·4	0·7	0·07
Pelvis	216	2·6	1·8	1080	233	22·7
Cervical vertebræ	128	1·5	2·9	1·5	0·2	0·02
Hips	228	2·7	2·2	880	201	19·5
Shoulders	196	2·4	2·2	0·7	0·1	0·01
Urinary tract	460	5·5	2·9	110	50·5	4·9
Cholecystography	120	1·4	4·5	13·5	1·6	0·15
Lumbo-sacral joint	380	4·5	2·7	81	30·8	3·0
Stomach	696	8·3	2·6	470	325	31·6
Intestinal tract (barium enema)	212	2·5	3·1	130	27·6	2·7
Excretion pyelography	188	2·3	4·2	590	111	10·8
Ribs	40	0·5	2·3	0·7	0·03	—
Dorsal vertebræ	200	2·4	2·3	17·2	3·4	0·3
Gall-bladder area	156	1·9	1·4	2·7	0·4	0·04
Retrograde pyelography	36	0·4	2·9	700	25·2	2·5
Bladder	52	0·6	1·2	240	12·5	1·2
Kidney	16	0·2	1·5	3·7	0·06	—
Liver	12	0·1	1·0	2·0	0·02	—
Total	8384	—	—	—	1028	—

[1] Average dose per examination, 123 milliröntgens.

pregnancy examinations, and the contribution resulting from mass radiography, as well as the increase in contribution to the gonads where children are concerned. The number of fluoroscopy cases is a very small proportion —approximately 1%—of the total number of cases dealt with in an X-ray diagnostic department, and it would therefore require a very large dose to the gonads to make a significant contribution from this cause. As the doses involved in fluoroscopy are usually much higher than those in radiographic examinations (Martin, 1947), the contribution has been set at 3% of the total. Approximately 25% of the Australian population is radiographically examined each year by mass-miniature units, and the corresponding contribution in a period of thirty years is estimated at six and 28 milliröntgens respectively for males and females. For obvious reasons the gonad dose per examination will be higher in children, but this is somewhat offset by the comparative rarity of the types of examination giving rise to the highest doses. An increase of 10% on the mean gonad dose is made to allow for the contributions from the radiographic examination of children. The allowance to be made for the dose to the fœtus, like that to the ovaries in pelvimetry and pregnancy examinations, is difficult to estimate, since examinations of this type tend to be carried out in specialist hospitals. By calculation from the figures of Martin and Williams (1946), of Osborn (1951), and of Stanford (1951), it is estimated that the fœtus receives 3*r* per examination. When some allowance is made for the examinations carried out in specialist hospitals, a figure of 15 milliröntgens is obtained for this contribution. The final total contribution to the gonads thus becomes 304 milliröntgens for females and 161 milliröntgens for males.

Other Sources Contributing to the Gonad Dose.

Apart from X-ray therapy and diagnostic X-ray examinations, there are a number of sources of ionizing radiations to which the population is exposed. The most important are natural radiation (cosmic rays and radiations from radioactive material in the ground), radioactive material in the body and occupational exposure.

In order to assess the hazard to the population from the point of view of genetic damage, one must relate the dosage received by diagnostic examinations to the totals received from these other sources. The unavoidable daily radiation due to cosmic rays and radioactive material in the ground is some two milliröntgens per week, and if we assume a generation to be thirty years, some 3*r* per individual will be received in this period. To this body radiation would add about another *r* in the same period. The estimated contributions due to occupational exposure, along with the contributions due to exposure from diagnostic examinations for Britain (Stanford *et alii*, 1952), for Sweden (Sievert, 1952) and for Australia are shown in Table V. It is interesting and, at first sight, surprising to find that, even in a country like Britain, where many workers are engaged in radiological services and atomic energy projects, the contribution due to diagnostic examinations is several times that due to occupational exposure. However, both sources give a substantially smaller contribution than that from unavoidable radiation. It is clear that errors in the assumptions involved in analysing the diagnostic contribution are unlikely to alter this result seriously.

If it is assumed that the doubling dose—that is, the dose to be given to each member of the population in a generation—at or before the reproductive stage to produce an induced mutation rate equal to the spontaneous rate is 50*r*, for which figure there is some experimental evidence, then the dose due to diagnostic work, shown in Table IV, would in Australian conditions increase the mutation rate by only 0·5%, which increase need not be a cause for alarm. Clearly, however, any increase in the hazard to the future of the race is more likely to arise from the increased use of diagnostic X-ray examination than from an increase due to those occupationally exposed. Particular care must be taken, therefore, in carrying out X-ray examinations, particularly those which involve large doses to the gonads. Especially should be mentioned those examinations related to women either desiring to have children or in the process of having children—in other words, such examinations as salpingography and X-ray examination in pregnancy, the latter also involving the fœtus.

Factors Affecting Dose to the Gonads in X-Ray Examinations.

It is pertinent to consider the factors in X-ray examinations which affect the dose reaching the gonads, and to see what can be done to keep this to a minimum.

When the gonads are within the field of irradiation, the factors affecting the dose reaching them are those discussed by Martin (1947). These are the kilovoltage, the filtration and the focus-film distance, all of which should be kept as large as is compatible with the performance of the unit and the obtaining of satisfactory radiographs. In the case in which the testes are in the field of irradiation, the conditions are exactly those which pertain on the skin, and the factors affect the dose to the testes in exactly the same way. Whenever possible it is recommended that a scrotum shield be used. In the case of the ovaries,

TABLE IV.

Doses Received by Gonads in Thirty Years.

Table IVA.

Country.	Source.	Female.		Male.	
		Dose. (Milliröntgens.)	Percentage of Total.	Dose. (Milliröntgens.)	Percentage of Total.
Australia.	Natural radiations	3000	69·5	3000	71·5
	Body radiations	1000	23	1000	24
	Occupational	20	0·5	20	0·5
	Diagnostic examinations	304	7	162	4
	Total	4304	100	4182	100
Britain.	Natural radiations	3000	70·5	3000	71·5
	Body radiations	1000	23·5	1000	24·0
	Occupational	60	1·5	60	1·5
	Diagnostic examinations	193	4·5	128	3·0
	Total	4253	100	4188	100

Table IVB.

Country.	Source.	Dose. (Milliröntgens.)	Percentage of Total.
Sweden.	Natural radiations }	4000 to 25,000	73 to 94
	Body radiations }		
	Occupational	<50	1 to 0·2
	Diagnostic examinations	<1000	18 to 4

increasing the kilovoltage and/or the filtration reduces the dose to the ovaries, as would be expected. However, the reduction obtained is not so great as in the case of the surface dose, since the overlying tissue itself acts as a filter. For example, if an 85 kilovolt beam and a focus-skin distance of 46 centimetres are used, changing of the filter from zero to one millimetre of aluminium reduces the skin dose by 33%, but the dose at the ovaries by only 16%. Again, changing the kilovoltage from 85 to 130, for a beam filtered with one millimetre of aluminium, reduces the surface dose by 78% and the ovary dose by 45%.

When the gonads are not in the beam and receive only scattered radiation, other considerations operate. It is almost superfluous to state that the gonads should be kept out of the direct beam whenever possible, and since, as is shown in Figure I, the dose fall-off with distance outside the edge of the field is rapid, a very large gain in protecting the gonads is obtained by small increases in the distance at which they are kept from the edge of the field. This points to the use of the smallest fields of irradiation consistent with the obtaining of the information required, and in this respect apparatus fitted with an adjustable diaphragm system is clearly to be recommended. Stanford (1951) has drawn attention to the reduction in dose received by the fœtal gonads in pelvimetry obtained by careful coning and positioning of the field on the patient.

The use of higher kilovoltages for radiography is being advocated frequently, voltages of the order of 120 to 140 kilovolts being suggested. While a substantial reduction in skin dose, and in gonad dose when the gonads are in the beam, can be achieved using these higher kilovoltages, it is pertinent to note that when the gonads are outside the direct beam the dose reaching them may be high, as the amount of scatter rises appreciably with increased kilovoltage. In general, the reduction in dose required to obtain a satisfactory film by the use of higher kilovoltages is such that, despite the increased amount of scatter, the dose to the gonads is smaller than in the corresponding case of a lower kilovoltage. However, in one case quoted in the literature relating to a lateral radiograph of the lumbar part of the spine, it is estimated that for the conditions under which the worker considers he obtained comparable radiographs, the dose to the ovaries is very slightly greater at 120 kilovolts than for a radiograph taken at 77 kilovolts.

The scattered radiation considerations are of particular importance in relation to children, since the distances involved are usually much smaller, and it has been observed that for chest radiographs the dose to the gonads in the case of children is some three or four times that for adults. In the case of the limbs and the extremities, careful coning and positioning are of importance. For example, the use of too large a field and bad positioning of the field in the radiological examination of a knee or a femur can result in a very high dose to the testes, while in general the dosage to the gonads is lower when the limbs are extended.

In conclusion then, it can be said that, in the light of our present information, and in the present state of our knowledge on the genetic effects of radiation, there appears little danger to the future of the race due to the dose contribution from diagnostic radiology, the increase in mutation rate being estimated at 0·5%. Muller (1954) estimates that a 12·5% increase in mutation rate could be tolerated by a population living under relatively primitive conditions of life and death, and suggests that a 25% increase would be approaching the danger level; such an increase would be brought about by a dose per generation of 20*r*. With certain reservations, he concludes that modern civilized society could tolerate a similar dose increment. While the average per-capita dose in a generation, as indicated by the foregoing analysis, does not approach this figure in Australia, there are indications that it is being approached in the United States (Public Health Service, Washington, 1952). However, X rays provide such a valuable diagnostic tool that it is almost certain that their use will increase, and in fact the present turn-over of patients in the X-ray diagnostic department of the Australian hospital from which the figures in Tables II and III are taken is already double that shown in the tables. Radiologists using the tool and clinicians seeking its aid should therefore consider carefully, in each case, the value of the information to be gained by its use before exposing a patient to X rays, particularly when the regions to be examined contain the gonads. In the use of the tool, consideration of the factors outlined above will enable the doses to the gonads to be kept to a minimum, while newer technical developments coming on the market, such as image amplifiers, will enable a substantial reduction in the doses involved to be made.

Summary.

The paper assesses the radiation contribution to the gene material of the population due to diagnostic X-ray examinations, and discusses its relevance to the hazard to the future of the race caused by radiation damage. Indications are that at present levels no danger exists. In view of the likely increase in the diagnostic use of X rays, discrimination in their use is recommended and means of keeping the gonad dose to a minimum are outlined.

Acknowledgements.

I am grateful to my colleagues, Dr. Basil Beirman and Dr. J. Hamilton Smith, for advice concerning techniques of X-ray examinations, to Dr. F. O'Donnell, Medical Superintendent, and Dr. Barbara Wood, of the Royal Melbourne Hospital, for permission to use the figures in Tables II and III, and to my secretary, Miss M. Comerford, who, in addition to preparing the manuscript, carried out much of the arithmetic involved.

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Reviews.

A Textbook of Neurology. By H. Houston Merritt, M.D.; 1955. Philadelphia: Lea and Febiger. Sydney: Angus and Robertson, Limited. 9½" × 6", pp. 746, with 181 illustrations. Price: £6 14s. 6d.

IT is always interesting to open a new text-book of neurology. The latest one to arrive is that by Dr. H. Houston Merritt. It is true, as he states in the preface, that neurology has returned more closely to the fold of internal medicine. The biochemical changes of hepatolenticular degeneration are cited to illustrate this, and a number of systemic diseases which may have neurological manifestations are included. The rarer diseases are succinctly yet adequately presented, with suitable references. Rare or uncommon though some are, their recognition is important. Behcet's triple syndrome and temporal arteritis are cases in point. The book, however, is far from being a mere repository of rarities, and the author's intention to write a text for medical students and physicians has been well carried out. Its scope is much the same as that of other well-known text-books, but Dr. Merritt has omitted preliminary chapters on anatomy and the examination of the nervous system, and gives his reasons for this. Necessary details of anatomy are given when the disease or syndrome is discussed. They are obviously necessary, for example, in any account of the arterial syndromes with which the author has long concerned himself. As was to be expected, his description of these is excellent. Epilepsy is fully and clearly dealt with. The advice given about the selection of drugs, their action and dosage is comprehensive. It is hoped, however, that in a new edition there will be a proper appreciation of the pathology and effects of cervical spondylosis on the cord. There is not in this one.

The book has 181 illustrations and 128 tables. The tables deserve special notice, for a great wealth of information, otherwise hard to obtain, is to be found in them. They give the book such value as a work of reference that it is to be recommended to any library or serious neurologist. Slight differences in American and British terminology, as in the muscular dystrophies and atrophies, could, but need not, cause more than transient confusion to those trained in the British school. Those so trained might think that here and there clinical description falls short of that of some of the older masters, but in what new text-book would it not? Misprints are apparently few in number. After "glioblastoma" the adjective "multiforme" is usually spelt "multiformi"; a few misprints were noted in quotations of German references. The volume is not bulky, printing and binding are very good, and the bibliography is a useful one.

Cardiac Symptoms in the Neuroses. By Doris M. Baker, M.D., F.R.C.P. (London); Second Edition; 1955. London: H. K. Lewis and Company, Limited. 7½" × 5", pp. 58, with seven illustrations. Price: 6s. 6d.

DR. DORIS BAKER published in 1942 a statistical account of three common symptoms encountered in patients presenting themselves at out-patient clinics as sufferers from heart disease, under the title "Cardiac Symptoms in the Neuroses". In the preface to a new edition she states she has found little reason to alter "the text", but that during and after the second World War the symptoms left submammary pain, sighing respiration and palpitation have increased in frequency, and require reemphasis. More than half of the patients seen in cardiac clinics have one or more of these familiar complaints, and Dr. Baker has investigated their frequency at the National Hospital for Diseases of the Heart and at the London Hospital. She claims that left inframammary pain is usually accompanied by hyperæsthesia and tenderness to palpation in the same area, extending to the angle of the left scapula. Hyperæsthesia, elicited by lightly dragging the head of a pin over the skin, was found in 68% of her patients, and tenderness in 45%. Of 332 consecutive patients, 42·3%, who were devoid of organic heart disease, complained of left inframammary pain, and 22% of those with organic heart disease suffered in this way. Intramuscular local anæsthesia is claimed to relieve the pain, and this appears to be the chief grounds for suspecting somatic muscle spasm or fatigue. A follow-up of sufferers from these symptoms shows long periods of remission, and no progress in the severity of the discomfort. The pain is uncommon as a sole manifestation of neurosis, and usually appears in company with the remaining components of Da Costa's syndrome.

Sighing respiration, another associated complaint, is more common than is generally realized, especially in women. Direct inquiry is often needed to reveal its presence. This type of breathing was termed "suspirious" by Walshe in

1873, and Dr. Baker retains the term. This symptom is exaggerated by fatigue and introspection, and while it may disappear for long periods, it will recur after shock or anxiety. Though Dr. Baker does not say so, it is, of course, a form of the hyperventilation syndrome, which in its more dramatic forms can lead to syncope and tetany as the result of respiratory alkalosis. Fluoroscopically, tonic contraction of the diaphgram has been observed prior to the appearance of the symptom, so that shallow respiration may lead to a compulsive sigh. The importance of this symptom lies in its usual association with other innocent symptoms such as intramammary pain and palpitation, and in the possible confusion in the mind of the doctor or patient with the dyspnœa of organic heart disease.

The third symptom investigated by Dr. Baker was palpitation. She points out the importance of determining precisely what the patient understands by this term and of the patient's own description of his feelings at the time of an attack. She refers to the varying threshold at which this symptom becomes consciously appreciated in different individuals and in the same individual at different times. As the result of examining the case sheets of 900 sufferers from palpitation, she concluded that the majority of those with organic heart disease and a primary complaint of palpitation suffered from hypertension, hyperthyroidism or paroxysmal tachycardia. It was nearly an even chance that a patient whose chief symptom was palpitation would have a normal cardio-vascular system, and in those with abnormal hearts, the above three conditions appeared with about equal frequency. Very few patients suffering from rheumatic heart disease gave palpitation as their chief complaint. Dr. Baker found that a considerable number of people could have extrasystoles without experiencing any palpitation, a fact with which all physicians would agree. She mentions dyspnœa, obesity, debility, the menopause and cigarette smoking as possible ætiological factors in some cases, but it is generally held that none of these are as important as the increased subjective sensitivity to any visceral stimulus which accompanies an anxiety state.

This little book is a straightforward, if superficial and rather elementary, consideration of the components of Da Costa's syndrome at the clinical and statistical level, and serves the useful purpose of reminding us of its frequency and its associations. There is still too much cardiac invalidism abroad, owing directly to unwarranted acceptance on the part of the doctor of the patient's own interpretation of symptoms.

The Year Book of Endocrinology (1954-1955 Year Book Series). Edited by Gilbert S. Gordan, M.D., Ph.D.; 1955. Chicago: The Year Book Publishers, Incorporated. 8″ × 5″, pp. 392, with 94 illustrations. Price: $6.00.

THE editorial comment in this Year Book is liberal, and it is supplemented by three special articles. This considerable addition to the straightforward abstracts from the year's literature will be welcomed by most readers as a necessary aid to keeping a sense of perspective in such a rapidly developing field of knowledge.

In the section on the pituitary gland the editor groups material first on the adenohypophysis (hypopituitarism and *anorexia nervosa*, Sheehan's syndrome, the Houssay phenomenon, selective pituitary failure, pituitary-parathyroid-pancreatic adenomatosis) and on the neurohypophysis and water metabolism with particular reference to *diabetes insipidus*. The chapter on the thyroid gland is divided into sections on tests of thyroid functions, hypothyroidism, hyperthyroidism and antithyroid drugs, exophthalmos, thyroiditis and cancer. The chapter on the parathyroid glands and calcium metabolism has sections on the calcium tolerance test, hyperparathyroidism, conditions simulating hyperparathyroidism, hypoparthyroidism, osteomalacia and osteoporosis.

The chapter on the adrenal glands covers a great deal of interesting material. The adrenal medulla has a section to itself, and the adrenal cortex is considered in relation to aldosterone, cortisone, hydrocortisone and corticotrophin, blood corticoid levels, cortical responsiveness, Addison's disease, androgenic hyperplasia, hirsutism, and tumours and hypercorticism. In addition there is a special contributed article entitled "Observations on the Sodium-Retaining Corticoid (Aldosterone) in Human Urine", by John A. Luetscher, junior, and Robert H. Curtis.

There is also a special article in the chapter on the reproductive system; in this Albert Segaloff discusses "Evidence Favoring the Concept of a Single Pituitary Gonadotrophin in the Human". The sections in this chapter are devoted to gonadotrophin and pregnancy, precocious puberty, intersexuality, the ovary and the testis.

In the chapter on carbohydrate metabolism are sections on pentose, fructose and galactose, electrolytes and carbohydrate metabolism, control of the blood sugar level, hypoglycæmia, diabetes and obesity, and *diabetes mellitus*.

Finally, in the section on endocrine treatment of neoplastic diseases is a special article by Donald E. Bernstein on the "Autotransplantation of Adrenal Cortex to Portal Circulation Combined with Oophorectomy and Adrenalectomy in Treatment of Metastatic Carcinoma of the Breast".

This Year Book Covers a great deal of ground and will be of invaluable aid to those who wish to keep up to date in the field of endocrinology.

Fractures and Joint Injuries. By Sir Reginald Watson-Jones, B.Sc., M.Ch.Orth., F.R.C.S., F.R.A.C.S. (Hon.), F.A.C.S. (Hon.); Volume II, Fourth Edition; 1955. Edinburgh and London: E. and S. Livingstone, Limited. 10″ × 6½″, pp. 640, with 904 illustrations, some in colour. Price: 120s.

THE second volume of this well-known author's work reaches the usual level of excellence of his other books. His standard of English prose is high, his meaning is clear and there is no waste of words.

The volume is profusely illustrated by excellent black and white, and some beautiful colour pictures. Captions are such that it is impossible for anybody to miss the main points of the pictures. The subject matter ranges over injuries to the upper and lower limbs, facio-maxillary injuries and injuries to the chest, the pelvis and the spine, together with a most stimulating chapter on rehabilitation after injury.

The author has kept pace with the development of new methods of treatment, but has not discarded the old and proven. He skilfully assesses the value of both, but is ready to advise against methods which have not lived up to early expectations. For example: in the third edition a good deal of space is given to a detailed and well-illustrated description of bonegrafting for ununited fracture of the scaphoid bone of the wrist; in the fourth edition this method is condemned in a short paragraph epitomized in the final sentence by these words: "It seems doubtful whether bone-grafting procedures offer any important contribution to the treatment of fractures of the carpal scaphoid." The use of intramedullary nails in the treatment of certain fractures of the shaft of the femur, humerus and ulna is countenanced by the author; he qualifies his approval, however, by pointing out that the method is fraught with serious dangers and pitfalls and is full of technical difficulties. He does not advise the method unless hospital conditions are impeccable and the surgical team is specially trained, particularly in regard to rigid aseptic technique. Then, with admirable impartiality, he claims that excellent results are obtainable by much more conservative methods. For example, he points out that first-class results with perfect alignment and little or no shortening can be obtained in cases of fracture of the shaft of the femur by treatment with extension on a Thomas splint. Very good descriptions are given, in detail, of the management of this fracture by both these methods.

This attitude of the author makes the book very valuable for the general practitioner, as well as for the specialist in traumatic surgery.

Some helpful aphorisms are used in the book, and these are valuable for teaching purposes. One apt example is: "No child with an injured elbow should be referred to a physiotherapy department." The reason for this is that uninhibited exercise by the child is the best treatment when an injured elbow has undergone repair. Passive movement is anathema in these cases. Another good example is: "Let us abandon forcible manipulation in the treatment of displacements of the upper femoral epiphysis." The reason for this is that such treatment is very seldom successful in reducing established displacement and is likely to lead to damage to the hip-joint, and movement of the joint is likely to decrease instead of to increase under such treatment.

It is interesting to read the author's summing-up of the indications for excision of a fractured patella. It is pointed out, of course, that the actual excision of the patella is only one phase of the operation. The most important part is the reconstitution of the quadriceps by accurate suture. He suggests that this operation should be reserved for fractures in middle-aged and elderly patients and for severely comminuted fractures in patients of all ages. His main line of reasoning is that in middle-aged or elderly patients, a comminuted fracture of the patella usually causes osteoarthritis, involving the patellar articular surface. This disabling condition can be avoided by excision of the fractured bone. It is particularly applicable to elderly people because it shortens the period of convalescence by enabling the patient to carry

out knee movements earlier than if the fragments were sutured together. His suggestion is that suture of the patella should be performed for fractures in young adults. It is recommended that when a fracture of the patella lies near the upper or lower poles, only the smaller fragment should be excised. He advises this modified operation even in young patients.

The subject of fracture of the spine with paraplegia is very well handled. A case is made out for occasional immediate laminectomy in certain cases. One indication mentioned is where progressively increasing neurological signs suggest the development of an epidural hæmatoma. Management of the paralysed bladder is described in some detail, with a particularly good account of high cystostomy with tidal drainage.

As a book of reference this volume is a necessity in the library of all those who handle injuries. It is written in such a pleasant manner and the illustrations are so good that it can be read through from cover to cover without any flagging of interest.

A Manual of Oral Embryology and Microscopic Anatomy. By Dorothy Permar; 1955. Philadelphia: Lea and Febiger. Sydney: Angus and Robertson, Limited. 10¼" × 7", pp. 110, with 49 illustrations. Price: 40s. 6d.

THIS volume has been written for students training as dental hygienists. These are ancillary workers who do not exist in Australia, but in the United States of America they are used to carry out dental prophylactic measures and to instruct patients in oral hygiene. The context of the manual is therefore written at a lower level than that offered to dental students. Nevertheless, it provides a very readable description of the embryonic development of the face and oral cavity, together with the histology of dental and gingival tissues and alveolar bone. The reproductions of pencilled drawings of views demonstrated under the microscope are excellent examples of what should be seen in a student's histological notebook. As stated in the introduction, a few of the statements made as facts may be somewhat controversial; but detailed discussion is deliberately omitted in order to avoid conflicts of ideas in the minds of those for whom the book is written.

Analytical Cytology: Methods for Studying Cellular Form and Function. Edited by Robert C. Mellors, M.D., Ph.D., with a foreword by Francis O. Schmitt, Ph.D.; 1955. New York: The Blakiston Division, McGraw-Hill Book Company, Incorporated. 9" × 6½", pp. 462, with 130 illustrations. Price: $15.00.

FASHIONS in research depend upon techniques. The classical approach through morphology is commonly regarded as a dead subject and the new approach has been *mainly chemical. The criticisms levelled at morphologists* is that function is ignored. At the other end of the scale, biochemists tend to ignore morphology. Between the two *extremes, physiologists have been trying to unite the various* lines of knowledge into a coherent pattern. Now, with the great technical advances which have been made in the last *few years, a new morphology is being written, the morph*ology of metabolism.

The book under review contains a critical appreciation of the newer methods of investigating cellular form and function. It has nine chapters each by experts. The subjects are divided into two groups. The first group deals with methods in the optical spectral region, and contains chapters on cytophotometry, histochemistry, phase contrast and other forms of interference microscopy, ultra-violet microscopy and microspectroscopy, and fluorescence microscopy. The second group is of more recent development and consists in the methods using electrons, radioactive isotopes and X rays. The subjects of electron microscopy, radioautography, historadiography and X-ray diffraction techniques are explained and reviewed in this section.

The volume is for the research worker and any other student of biology who needs a reference book wherein he may keep abreast of recent developments.

This is an exciting era of biological research to which the physical sciences are contributing. By these methods the various components in the cell can be identified, though as yet we have a very hazy idea of their meaning. The newer methods of research are for the first time integrating morphology with function. In due course, physiological laws applicable to the cell as the basic unit of the organism may be expected.

The figures are excellent in this volume and the features they illustrate are well portrayed. Each chapter has a comprehensive list of references embracing those of historical as well as contemporary interest.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Differential Diagnosis: The Interpretation of Clinical Evidence", by A. McGehee Harvey, M.D., and James Bordley III, M.D.; 1955. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. 9¾" × 6", pp. 680. Price: £6 10s.

The several chapters are illustrated by cases discussed at clinico-pathological conferences.

"The Practice of Dynamic Psychiatry", by Jules H. Masserman, M.D.; 1955. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. 9¾" × 6", pp. 820. Price: £6.

Deals first of all with the rationale, objectives and methods of the psychiatric interview and then with the various syndromes of behaviour disorder.

"Neuro-Vascular Hila of Limb Muscles", by James Couper Brash, M.C., M.A., M.D., D.Sc., LL.D., F.R.C.S.Ed., F.R.S.E.; 1955. An atlas with 30 coloured plates. Edinburgh and London: E. and S. Livingstone, Limited. 10" × 7½", pp. 100, with many illustrations. Price: 30s.

Contains data on the sites and modes of entry of the principal arteries to the limbs that the information may be useful in the diagnosis and treatment of injuries.

"Systemic Associations and Treatment of Skin Diseases", by Kurt Wiener, M.D.; 1955. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical), Limited. 10" × 7", pp. 556, with 90 illustrations. Price: £9 7s.

This book is complementary to the author's "Skin Manifestations of Internal Disorders (Dermadromes)".

"Mysterious Waters to Guard: Essays and Addresses on Anæsthesia", by Wesley Bourne; 1955. Oxford: Blackwell Scientific Publications. 9¾" × 6", pp. 418. Price: 42s.

The addresses number 34 and cover a large range of subjects.

"The Mental Hospital: A Study of Institutional Participation in Psychiatric Illness and Treatment", by Alfred H. Stanton, M.D., and Morris S. Schwartz, Ph.D.; 1954. London: Tavistock Publications, Limited. 9" × 6", pp. 511. Price: 35s.

The book is the report of a three-year socio-psychiatric study of a ward in a psychiatric hospital.

"Pathology for the Surgeon", by William Boyd, M.D. (Edin.), Dipl.Psychiat. (Edin.), F.R.C.S. (Canada), F.R.C.P. (Lond.), M.R.C.P. (Edin.), F.R.S. (Canada), LL.D. (Sask.), D.Sc. (Man.), M.D. (Oslo); Seventh Edition; 1955. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. 10" × 7", pp. 744, with 547 illustrations. Price: £6 5s.

The first edition of this book was published in 1925.

"Cardiology Notebook: For Preliminary Instruction in Medical Curricula", edited by Alfred P. Fishman, M.D., Chairman, M. Irenè Ferrer, M.D., Rèjane M. Harvey, M.D., John H. Laragh, M.D., Dickinson W. Richards, M.D., and Josephine S. Wells, M.D.; College of Physicians and Surgeons, Columbia University; 1955. New York and London: Grune and Stratton, Incorporated. 10" × 8", pp. 98, with 18 illustrations. Price: $2.50.

For the medical student to make available to him a few basic examples of the methods and language of cardiology.

"Problems of Consciousness: Transactions of the Fifth Conference, March 22, 23 and 24, 1954, Princeton", edited by Harold A. Abramson, M.D.; 1955. New York: Josiah Macy Junior Foundation. 9" × 6", pp. 180. Price: $3.50.

Among the subjects dealt with were three dimensions of emotion, anxiety, the role of the cerebral cortex in the development and maintenance of consciousness, and anæsthetics.

The Medical Journal of Australia

SATURDAY, NOVEMBER 12, 1955.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words of phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

AVICENNA.

AVICENNA, whose real name was Abu Ali al-Hussein ibn Abdallah ibn Sina, described by Castiglioni as the most illustrious physician of the Golden Age of Arabian medicine, lived from A.D. 980 to 1037. He had a profound effect on medical learning and was remarkable in other fields than medicine. McCarrison writes that he was "one who trod the primrose path at ease and died in the prime of life from the effect of its pleasures". Castiglioni, on the other hand, refers to "his stormy life, which led him through many transitions and great sufferings to death in the fifties". An opportunity to study the life and achievements of Avicenna arises from the fact that the New York Academy of Medicine held in 1954[1] a meeting to commemorate what is described as his thousandth anniversary. In this journal on April 19, 1952, there appeared a most interesting article on Avicenna by Professor W. S. Dawson, of Sydney, in which he explained that confusion had arisen between the Mohammedan and the Christian calendars, and that Avicenna's millennium was the year 1951. At the New York meeting four papers were presented. Iago Galdston, the Executive Secretary of the Committee on Medical Information of the Academy of Medicine, acted as chairman and read an introductory paper. Ali Gholi Ardalan, Ambassador and Permanent Representative of Iran to the United Nations, discussed "What Avicenna Means to the Persians"; George Sarton, Professor of History of Science at Harvard University, dealt with "Avicenna, Physician, Scientist and Philosopher"; Arthur Upham Pope, Chancellor Emeritus of the Asia Institute Association, read a paper entitled "Avicenna and His Cultural Background".

Avicenna (three of the authors refer to him as Ebn Sina) was a most precocious youth. Ardalan began his address by referring to the cultural history of Islam and to the part which the Persian element played in the formation and development of the Moslem contribution to world culture and learning. He states that the Persian intellectual manifestations produced the greatest works in science, mathematics, astronomy, theology, philosophy, history and medicine in the Islamic world. At the age of ten Avicenna had a knowledge of the Koran, and he was introduced to secular learning "by Ismailist propagandists who had been received into his father's house". After studying Islamic law, he was taught logic, geometry and astronomy; he then went on to physics, metaphysics and medicine. Sarton thinks that his scientific curiosity was probably excited during his youth by the fact that his father was an Isma'ili. Be that as it may, by the age of eighteen he had cured the Sultan of a disease and devoted more and more time to medicine, and he became not only the Sultan's physician, but also his general adviser. He seems to have known something of psychology, for Pope tells of how he was once challenged to cure on the instant a girl serving in the royal apartments who was bent over and could not straighten up again. He ordered her veil to be removed, and although this put her in "an anguish of embarrassment" her body was still locked and immobile. "'Off with her skirt', commanded Ibn Sina; the girl in a spasm of emotional shock straightened up and disappeared."

We should look first at Avicenna's philosophy and then at his medicine. Sarton asks where he got his inspiration and his pabulum. He points out that the oldest sources were Greek. He is said to have read the "Metaphysics" of Aristotle no less than forty times and to have understood it only when it was made clear to him by al-Farabi's commentary. In addition he studied the "so-called" "Theology of Aristotle" which was really a late Neoplatonic compilation, mainly derived from Plotinos's "Enneads". Sarton writes that Avicenna's philosophy is focused on the theory of being and the difference between essence and existence. The essence is the "quiddity", the raison d'être, of an object. Existence is an accident which may be added to it or not. The essence is necessary, existence is accidental. In God alone are essence and existence united; God is necessary, all the rest is only possible or potential. One of Avicenna's main problems, Sarton continues, was to harmonize Aristotelian (or Plotinian) philosophy with Muslim theology—for example, how to reconcile the Aristotelian concept of the eternity of the world with the Muslim idea of creation *ex nihilo*. His solution was "a strange compromise"—the world is eternal but God is anterior to it. The Creator is Truth, Love, Life. He is pure intelligence. Creation issues from Him as an intellectual flux; it is at one and the same time a transmission of being and a radiation of intelligence. Discussing the influence of Avicenna's philosophy, Sarton tells us that his philosophy was known in the West, half a century before that of Aristotle. Pope draws attention to the fact that Avicenna's vast knowledge was balanced by a realization of the limits of knowledge—a mark of wisdom. His poetry reveals this. A quatrain of his, subsequently attributed to Omar Khayyám, and made famous by Fitzgerald's adaptation, reads:

> Up from Earth's Centre through the Seventh Gate
> I rose, and on the throne of Saturn sate,
> And many a Knot unravelled by the road;
> But not the Master Knot of Human Fate.

Avicenna wrote many medical books; the best known and most important is his "Canon of Medicine". Professor Dawson dealt at some length with Avicenna's medical

[1] *Bull. New York Acad. Med.*, April, 1955.

activities and reproduced some important illustrations from his works. We do not intend therefore to do more than refer to historians' comments on the "Canon". Castiglioni writes that the "Canon" may best be regarded as a magnificent attempt to coordinate systematically all the medical doctrines of Hippocrates and Galen with the biological concepts of Aristotle. The Canon consists of five large books. The first deals essentially with theoretical medicine, the second with simple medicaments, the third with diseases and their treatment, the fourth with general diseases and the fifth with the composition and preparation of drugs. Castiglioni states that Avicenna's medical science is founded on the humoral doctrine of Hippocrates. "He does not admit the slightest doubt. He legislates in medical matters with an absolute authority, as is shown in that title he selected, the Canon, with the idea that it should constitute an immutable law. The clarity of the clinical histories, the accuracy of the therapeutic indications, constructed logically and without dangerous exaggerations, and the elegance of his forcible style were sufficient to confer on this book up to the end of the seventeenth century an almost indisputable authority in the minds of physicians of all countries. It also led to the publication of innumerable commentaries." McCarrison prefers to look at the long-range effect of the work. He holds that on the whole the influence of the "Canon" upon mediæval medicine was bad, in that it confirmed physicians in the pernicious idea that ratiocination is better than first-hand investigation. "It also set back the progress of surgery by inculcating the novel doctrine that the surgical art is an inferior and separate branch of medicine and by substituting the use of the cautery for the knife."

Passing by Avicenna's history of ups and downs—he had his share of adversity, which in those days could be most devastating—we must try to formulate some general conclusions that may possibly stimulate us. Failing this, the recent "commemoration" will be of little use to us. Avicenna was born in the Golden Age of Islam. Its culture was derived in substance from the ancient civilizations of the Near East and had been supplemented by additions from India and the Far East. The Arab contribution to them was "a new ardor and force of will". Pope is undoubtedly right when he states that in the widespread Islamic culture there were elements without which Avicenna could not have been Avicenna. Probably his outstanding qualities that will set him apart for emulation today were his intensity of purpose and his devotion to truth as he saw it. The differences of opinion about his easy or difficult times in life do not matter; the qualities named were dominant. In another thousand years his memory will still be honoured.

Current Comment.

"PUROMYCIN" AND NEOPLASMS.

"PUROMYCIN" ("Stylomycin") is an antibiotic derived from *Streptomyces albo-niger*; it has an inhibitory action on some bacteria and trypanosomes; it has also been found to have an appreciable inhibitory action on two mammary adenocarcinomata of mice, and on a chick embryo glioblastoma. Accordingly, Jane C. Wright, Vera B. Dolgopol, Myra Logan, A. Prigot and L. T. Wright[1] tested it on 51 patients with incurable neoplastic disease. Two had Hodgkin's disease, the remainder had various carcinomata. The details of treatment are unimportant, and none of the patients showed any permanent improvement—all died eventually. What is possibly important is that 14 of these patients had temporary slight regression in the size of their tumours after twenty-one or more days' treatment, with no evidence that anything other than the "Puromycin" could have caused the regression. The authors suggest that this result justifies further investigation of the chemical structure of metabolic end-products of this antibiotic with reference to their possible chemotherapeutic effects on neoplasms. Unfortunately investigations like this are lengthy and costly, and many substances have been reported to have similar effects; only too probably, most will not be followed up, and perhaps some effective agent may be left undiscovered. On the other hand, there may come a time when a large number of partly effective substances have been discovered, and when some methodical worker may survey them and pick out a common factor which will give a useful lead to further successful investigations. At any rate, there are many strong reasons why this type of screening for anti-carcinoma agents should be persisted in, so long as men and women of goodwill can be found, among the unfortunates with incurable cancer, who will submit to the unpleasant side-effects of treatment ("Puromycin", for instance, is reported to cause nausea, vomiting and diarrhœa, which can be major trials to somebody dying of cancer) and to the strain of raised and then dashed hopes.

MYASTHENIA GRAVIS.

ASSESSMENT of the clinical progress of *myasthenia gravis* is difficult, because of the frequency with which spontaneous remissions occur. It has even been estimated that treatment with neostigmine might reduce the frequency and duration of spontaneous remissions. Recent opinions from both the United Kingdom and the United States of America are in favour of thymectomy as the treatment of choice, but F. R. Ferguson, E. C. Hutchinson and L. A. Liversedge[2] have analysed a series of 85 patients with *myasthenia gravis* treated at the Manchester Royal Infirmary during the past twenty-two years, only ten of whom were submitted to surgery, and have concluded that a diagnosis of *myasthenia gravis* need not be regarded as an automatic indication for immediate thymectomy. The relevant figures show that of the 85 patients only ten were considered to need surgery; nine of the others have died, six have been lost sight of, and of the remaining 60, who have been followed up for from two to twenty-two years, 42 are performing full work, nine suffer some restriction, six have definite disability and three are quite disabled. Of the ten patients treated by thymectomy six have died, one each of the surviving four is in the groups of full work, some restriction, definite disability and full disability. Of the nine medically treated patients who died, three died of cancer, two of thymoma, three of myasthenia, and one was not traced; all of the six surgically treated patients who died did so of myasthenia.

Medical treatment in this series consisted in giving an optimal dose of neostigmine (determined by trial and error) with the occasional addition of ephedrine, guanidine and potassium chloride; in the rare instances of neostigmine intolerance, and when early morning weakness was marked, pyridostigmine was found of value. From the details of these cases, the authors conclude that once the diagnosis has been established, there should be a period of observation, with neostigmine treatment, before assessing the severity and probable course of the disease and the possible necessity for thymectomy. If the condition is initially confined to the ocular muscles, and remains so

[1] *Arch. Int. Med.*, July, 1955.
[2] *Lancet*, September 24, 1955.

confined for two or three years, there is a good chance that the disorder will remain local and will produce little or no disability, so that thymectomy would probably be unnecessary; but if the condition is generalized at an early stage and cannot be controlled adequately with neostigmine, or if the ocular form extends to the general form, thymectomy is indicated. *Myasthenia gravis* is a comparatively rare condition, and the well-balanced advice on its treatment which this article offers should be of value to those who meet the disease only once or twice in a lifetime.

FRUCTOSE.

IT has long been known that fructose can be metabolized by a diabetic patient, and its use in the feeding of such patients has often been recommended. Fructose is absorbed from the intestinal tract much more slowly, and it is removed from the blood more quickly than is glucose. Glucose administered by mouth causes a temporary rise in the blood sugar content of the normal person and a prolonged rise in the diabetic subject. Fructose causes a very slight or no rise in the blood sugar content in either the normal or the diabetic person. Before one can assess the clinical value of fructose it is necessary to know what happens to it after absorption. During the past few years much work has been done on the metabolism of fructose and a fairly clear account may now be given; A. E. Renold and G. W. Thorn have done this and have given an appraisal of the clinical usefulness of fructose.[1] Part of the fructose is metabolized through the usual pathways of glycolysis through hexose phosphates to pyruvic acid and thence to carbon dioxide and water through the Krebs cycle or to lactic acid or other substances including fats. A large part of the fructose can be metabolized by another pathway which does not require the action of insulin as does the glycolytic pathway. Five reactions peculiar to fructose have been described. (i) Fructose can be phosphorylated in position 6 in the presence of hexokinase and ATP. It thus enters the glycolytic pathway. Brain hexokinase, the most studied, has a much greater affinity for glucose than for fructose and glucose greatly inhibits the phosphorylation of fructose by this enzyme. The importance of this will be seen later. (ii) In liver and muscle fructose can be phosphorylized in position 1 by a specific fructokinase. Fructose-1-phosphate cannot directly enter the glycolytic pathway and conversion to fructose-6-phosphate does not take place to a significant extent. (iii) Fructose-1-phosphate can be split by a specific enzyme to two three carbon compounds, one of which is phosphorylated, the other not (dihydroxyacetone phosphate and glyceraldehyde). (iv) Glyceraldehyde can be converted to glyceraldehyde phosphate. These two phosphates are in the glycolytic pathway. (v) Fructose-1-phosphate may be phosphorylated to fructose-1-6-phosphate and thus converted into glycogen or enter the glycolytic pathway.

Which of these reactions is the most important in the metabolism of fructose? Before this can be answered we need to know the extent of fructose utilization in different organs. The greater part of the fructose is metabolized in the liver which takes up fructose from the blood at a much greater rate than it does glucose. The metabolism here is mainly through reactions (ii), (iii) and (iv) and the rate of conversion to lactic acid *et cetera* is much greater than that of glucose. The enery value of fructose then, in smaller molecules, is very rapidly made available if the liver is normal.

In the presence of glucose the brain cannot adequately utilize fructose, which does not prevent hypoglycæmic symptoms. The position in regard to muscle is somewhat doubtful. At best fructose utilization by muscle is slow. Experiments have shown that in the presence of equal concentrations of glucose and fructose the rat diaphragm metabolizes six to seven times more glucose than fructose in the formation of glycogen and about three and a half times more glucose than fructose in the conversion to carbon dioxide and water. Fructose tolerance is greatly decreased in extensive liver damage, but this is a late manifestation. The metabolism of fructose in diabetic persons has frequently been studied and it has been demonstrated that tissues from diabetics utilize fructose at nearly normal rates. Insulin then is not necessary at least for reactions (ii), (iii) and (iv) and for the metabolism of the greater part of the fructose. To sum up, fructose is metabolized mainly in the liver and by reactions (ii), (iii) and (iv) which do not require the presence of insulin. When fructose is administered intravenously a much larger portion of the administered sugar may be expected to enter the liver cells than in the case of glucose. This may explain the greater protein-sparing action of fructose and the favourable effect of fructose in some hepatic intoxications.

The rapidity of uptake by the liver of fructose indicates its use as a substitute for glucose whenever a sugar must be administered rapidly and whenever the renal threshold for glucose is exceeded leading to glucose wastage. Fructose can be useful during the first hours of treatment of diabetic acidosis, for it takes some time before insulin administration affects the deranged glucose metabolism in the liver, whereas fructose acts immediately. It is still uncertain whether fructose has any useful place in long-term therapy of diabetes. It may contribute to the control of anomalies of lipid metabolism in the diabetic liver and this is worthy of investigation. The rapid and almost exclusive utilization of fructose by the liver may be used to assess the functional state of the liver.

The administration of large amounts of fructose may have certain clinical dangers. It is not justifiable to assume that the liver will convert enough fructose to glucose to supply the needs of brain and muscle which themselves cannot adequately utilize fructose. In patients receiving insulin and fructose the rate of removal of glucose from the blood-stream may exceed the rate of glucose formation from fructose, and dangerous hypoglycæmia may result, which would be masked in the blood sugar estimations by the fructose, which reacts in the estimations exactly as does glucose. Because of the rapid metabolism of fructose when large doses of fructose are given intravenously sufficient lactates and pyruvates may accumulate to causes significant acidosis.

[1] *Am. J. Med.*, August, 1955.

DIABETES.

THE development of premature arteriosclerosis in diabetics has been the subject of controversy for many years. J. W. Headstream and J. T. Wortham[1] hold that altered adrenal cortical function may well be responsible for arteriolar degeneration—that high blood sugar levels cause stimulation of the adrenal cortex, and, moreover, that insulin hypoglycæmia, relative or absolute, is also stimulating to the adrenal cortex, and that the wide fluctuation in blood sugar levels in diabetics causes corresponding fluctuation in adrenal cortical secretion, especially when the long-acting types of insulin are used. These workers accordingly performed bilateral total adrenalectomy on seven patients with severe diabetes and advanced vascular disease, maintaining them thereafter with suitable doses of cortisone. Two patients showed considerable general improvement, two showed some improvement, and three died, one of adrenal insufficiency after initial improvement, one of cerebral vascular disease and progressive renal failure, and one for no stated reason after a period of slight improvement. In every instance less insulin was required, post-operatively, to control the diabetes. It would seem that the treatment is justifiable in the presence of severe and progressive vascular deterioration, provided that it is carried out before the vascular changes have gone too far.

This series links up with observations made by W. P. N. Jackson[2] in a paper entitled "A Concept of Diabetes".

[1] *J. Urol.*, July, 1955.
[2] *Lancet*, September 24, 1955.

Jackson suggests that diabetes may be either inherited, congenital or acquired, and that the pre-diabetic state is present from birth, manifesting itself from time to time under the stimulus of pregnancy, infections, or treatment with cortisone, and perhaps becoming permanent, clinically, after one or more such episodes, or after the development of acromegaly or Cushing's syndrome. Jackson also suggests that pregnancy, with the strain it imposes on the pancreas, is diabetogenic not only in the predisposed woman, but in the fœtus too. He instances the frequency with which diabetic women produce babies that are stillborn, or are gigantic or "Cushingoid", or who grow too tall or have an abnormal vascular system, or who develop diabetes. He gives tables and graphs which support this statement, and discusses the interlocking action of growth hormone, insulin, and corticoids, both in the mother and as regards the manner in which they affect the fœtus.

Possibly complementary to these two papers are the observations of A. Stuart Mason[1] on six women, none of whom was suffering from diabetes, who underwent total adrenalectomy for the treatment of carcinomatosis. They received compensatory medication with adrenocortical steroids. Studies of their metabolism showed that their responses were normal and similar to those of patients undergoing other types of operation not involving the adrenals. That in the non-diabetic patient compensated adrenalectomy produces no metabolic changes, while similarly compensated adrenalectomy in the diabetic produces a trend towards normal metabolism, is a finding which further links up the connexion between pancreatic function and adrenal secretion.

INFECTIOUS HEPATITIS.

Two interesting papers on infectious hepatitis have recently appeared. John R. Neefe and seven colleagues[1] have made a survey of: (i) 271 ex-servicemen who had suffered from acute viral hepatitis with jaundice from two to seven years previously; (ii) 146 civilians with a history of having had the disease some ten years previously; (iii) 138 ex-servicemen and 46 civilians who had been exposed to the risk of infection during epidemics, but who had had no apparent attacks; and (iv) 168 ex-servicemen and 142 civilians with no history of exposure to epidemics, and with nothing in their histories to suggest any affection of the liver. A complete examination of these people was undertaken to determine the degree of demonstrable liver damage referable to a previous attack of infectious hepatitis. It was concluded that demonstrable severe or active chronic liver disease was not significantly higher among persons with a previous history of hepatitis with jaundice than in those with no previous history of recognized hepatitis.

The second paper, by Thomas C. Chalmers and twelve associates,[2] concerns clinical trials conducted by the United States Army on the effects of bed rest and diet in the treatment of patients suffering from acute infectious hepatitis with jaundice or persistent dark urine. The first study was in four sections; half the patients were kept at strict bed rest, half were allowed to get up and move about the hospital at will; across these two groups, half were allowed to eat whatever they wished from a nutritious diet, while the other half were forced to eat, regardless of anorexia, a minimum diet of 3000 calories a day, 20% of which was in the form of protein, and were given supplements of choline and vitamins. Those on enforced bed-rest improved no more rapidly than those allowed up, but those on forced diet with a high-protein content improved more rapidly than those allowed to eat only what they wanted. In a second study, patients on a 19% protein diet had a shorter duration of hepatitis than those on an 11% protein diet; whether they ate 3000 or 4000 calories daily, and whether they had supplements of choline and extra vitamins or not, made no difference. Undue activity and extra exertion, as distinct from just being allowed up and about at will, delayed cure.

The total effect of these two papers is a comforting one, in that the second offers evidence that in infectious hepatitis a high-protein diet is beneficial, and that strict bed rest, with all the extra nursing it involves, is unnecessary, so long as the patient does not over-exert himself, and the first paper demonstrates that the disease causes no permanent liver damage.

[1] *Lancet*, September 24, 1955.
[2] *Ann. Int. Med.*, July, 1955.
[3] *J. Clin. Investigation*, July, 1955, Part II.

SKIN PHOTOSENSITIVITY.

MANY substances can render the skin hypersensitive to sunlight; among them are the sulphonamides, many coal-tar derivatives, various dyes, certain barbiturates when given parenterally, and, when applied to the skin, some of these drugs, and the juices of various plants, notably parsnips. John Godwin Downing[1] points out that the skin is fundamentally too sensitive to strong sunlight as it is, and that when hypersensitivity due to various agents is added, although the skin reactions are usually temporary, there are cases in which more serious results follow. He suggests that *lupus erythematosus* may commence in this way. As a general argument, Downing states that measures to protect the skin from the effects of prolonged exposure to strong sunlight are well worth considering. He discusses the results of experiments on the screening properties of various creams, and concludes that 15% para-aminobenzoic acid, 5-isobutyl para-aminobenzoate and 7·5% tannic acid all afford excellent protection against solar erythema, although occasionally para-aminobenzoic acid may cause dermatitis.

Downing also discusses the effect of mepacrine hydrochloride and chloroquine diphosphate, which, when taken internally, reduce the skin's sensitivity to sunlight, and are effective in the treatment of actinic dermatitis. Moreover, both of these drugs have been reported as being valuable in the treatment of *lupus erythematosus*; chloroquine has even been reported on favourably as a treatment for some cases of *lichen planus* and verruca, and mepacrine for *pemphigus foliaceus*. However, these last effects are not supported by controlled experiments—and children in the tropics, taking chloroquine regularly as a malaria prophylactic, still seem to suffer their fair share of warts. Nevertheless, Downing's argument is very sound; it would be interesting to see whether small doses of chloroquine during the surfing season would do anything to reduce the incidence of severe sunburn, for instance.

CHLOROPHYLL.

THE general impression has been that chlorophyll has had its day, but Lawrence W. Smith[2] has presented a report on "The Present Status of Topical Chlorophyll Therapy" which contains some very interesting matter. Smith points out that chlorophyll ranks with the other porphin derivatives, hæmoglobin, catalase, peroxidase and the cytochromes, in that it is concerned in the fundamental mechanism of oxidation reduction. Over 800 derivatives of chlorophyll have been described, most of only academic interest and many therapeutically inert, but some of definite value. The action of the water-soluble chlorophyllins on bacterial metabolism is responsible for a deodorizing effect in contaminated wounds; they are not effective contact deodorants nor do they "adsorb" odours. When, by chelation, chlorophyll's magnesium is replaced by sodium and copper, it has a measurable effect in hastening the growth of fibroblasts in tissue cultures, which is the basis, together with its activities in modifying bacterial metabolism, of its power to stimulate the growth

[1] *New England J. Med.*, August 11, 1955.
[2] *New York State J. Med.*, July 15, 1955.

of healthy granulation tissue. The effect on bacteria is primarily in the direction of destroying or decreasing the toxicity of their metabolic products.

Barnard showed that certain chlorophyll derivatives can delay, or even prevent, red cell hæmolysis in oxalated or citrated blood; in higher concentrations they will inhibit, *in vitro*, agglutination due to Rh "blocking antibodies"; they also inhibit the action of necrosin. Smith concludes with the suggestion that chlorophyll offers a suitable starting-point for the synthesis of antibiotic-like substances of specific value. His enthusiasm for this much-maligned substance is tremendous, and might be regarded as exaggerated, except that he has assembled a large array of references from impressive sources to support it.

"MAREZINE" AND POST-OPERATIVE VOMITING.

AN investigation of the effect of "Marezine" (N-benzhydryl-N'-methyl piperazine dihydrochloride) on post-operative vomiting has been made by Sara J. Dent, V. Ramachandra and C. R. Stephen.[1] "Marezine" is stated to have negligible side effects. In this investigation 2000 patients were given no "Marezine", and served as controls. One thousand patients, all over two years of age, receiving various types of anæsthesia, were given 50 milligrammes of "Marezine" subcutaneously (proportionate doses for children) thirty to sixty minutes prior to the expected time of termination of anæsthesia. The results were as follows: after ethyl ether, 38·5% of the controls and 25·8% of the treated subjects vomited; after "Pentothal Sodium. of the controls 20·1% vomited as against 13·3% of the treated subjects; after cyclopropane, controls 34·6%. treated subjects 39·8%; after spinal anæsthesia, controls 11·1%, treated subjects 5·8%; and after regional anæsthesia, controls 4·3%, treated subjects nil. The authors attribute to "Marezine", given in this way, an overall reduction in post-operative vomiting from 27·2% to 20·7%. Actually, since there was an increase in vomiting following cyclopropane, it could be stated that the treatment is unsuited to this anæsthetic; if we consider only the other types tested, the reduction was from 26·3% to 18·0%. This is a reduction of some 31·0% in total vomiting, which is considerable; whether anæsthetists would consider it worth while is a matter for them.

SILICONES AND SKIN PROTECTION.

WITH the increasing use of irritating substances in industry there has arisen a much greater need for protecting the skin—not with gloves, but by covering the exposed surfaces with a protective film. Many "barrier creams" have appeared, some of general value and some with a specific application. The silicone compounds are very versatile substances, two of their most important properties being their ability to repel water and their chemical inertness. When they are applied to the skin, they produce no adverse effect whatever. Consequently, they have been widely used as barrier coatings. C. R. Denton, D. J. Birmingham and V. B. Perone[2] have devised a method of testing skin protectives, and have screened 20 of these; six were commercial silicone-containing skin protectives, ten were commercial protectives which contain no silicone, four were industrial silicone oils and greases, and the last was white soft paraffin, which was used as a standard reference barrier film because of its uniformity, relative inertness and known high value against water, weak acids and alkalis.

Denton and his associates devised a modification of the Schwartz testing method, in which the challenging liquid was allowed to penetrate a standard film of the substance under test. Indicators measured the degree of penetration, or else dyes were added to the liquids. The challenging liquids were water, 1·0% aqueous solutions of soap and a synthetic detergent, 0·25N solutions of sodium hydroxide and hydrochloric acid, commercial cutting oils and liquid paraffin.

White soft paraffin was found to be a very effective barrier; two of the commercial silicone protectives were superior, two were fair, and two were poor. Silicone fluids were ineffective, but silicone greases were very efficient. Non-silicone protectives were inferior to soft paraffin and to the two best silicone protectives. Strangely, a silicone ointment based on soft paraffin was inferior to soft paraffin alone. The most successful challenging agent throughout was a synthetic anionic detergent.

This is a most satisfactory report. The general impression it gives is that silicones are not certain protectives; in fact, the probability is that the vehicle may be more useful than the silicone itself. Non-silicone protectives give a generally better performance than those containing silicones. Finally, soft white paraffin gives, for general purposes, adequate protection at a higher level than most of the more elaborate preparations.

LOBELINE AS A DETERRENT TO SMOKING.

SMOKING is a notoriously hard habit to break, and even patients with conditions in which cessation of smoking is essential to their well-being find it always hard, and often impossible, to give up. In some people the withdrawal symptoms are severe and prolonged, and these need some aid in maintaining their determination. Lobeline has been used for many years as a deterrent, with varying success. Now a preparation ("Bantron") has appeared which seems to neutralize the unpleasant side effects of lobeline, and to reinforce the deterrent effect, so that a much smaller dose is effective. G. W. Rapp and A. A. Olen[1] have carried out a series of controlled tests with this preparation, and have found that "Bantron" tablets, which contain two milligrammes of lobeline sulphate and 100 milligrammes of a mixture of slow-acting and fast-acting antacids, cause a diminution in the number of smokes per day (to about one-fifth after a week) when no conscious attempt to reduce smoking was made, and helped 80% of subjects to refrain deliberately from smoking after a week. Tested separately, neither the lobeline nor the antacids had any comparable effect. There were no side-effects from the treatment. If this preparation is as good as this report indicates, it should prove a boon to those who have been given "doctor's orders" not to smoke, or to those who fear lung cancer, or even to those who wish to save money.

THE RETIREMENT OF DR. H. E. MACDERMOT.

THE issue of *The Canadian Medical Association Journal* for July 1, 1955, brings news of the retirement of its editor, Dr. H. E. MacDermot. Dr. MacDermot became editor in 1942, but he began his association with the journal thirty-one years ago when Dr. A. D. Blackader was editor. Blackader was succeeded by Dr. A. G. Nicholls, and Dr. MacDermot took over from him. *The Canadian Medical Association Journal* has had an important influence on medicine in Canada and the North American Continent. It is the official organ of the Canadian Medical Association which is affiliated with our own British Medical Association. Dr. MacDermot has shown wisdom in this conduct of the Canadian journal and Canada is in his debt. Fortunately the journal will not be completely deprived of his wise counsel, for he will continue to serve it as a consultant. He will have the good wishes of all connected with THE MEDICAL JOURNAL OF AUSTRALIA, which has enjoyed his friendship over the years, and of the many friends whom he has made in this Commonwealth.

[1] *Anesthesiology*, July, 1955.
[2] *Arch. Dermat.*, July, 1955.

[1] *Am. J. Med. Sciences*, July, 1955.

Abstracts from Medical Literature.

PATHOLOGY.

The Pathogenesis of Fibrocystic Disease of the Pancreas.

R. A. ALLEN AND A. H. BAGGENSTOSS (*Am. J. Path.*, March-April, 1955) have studied eight cases of fibrocystic disease of the pancreas by examining serial sections of the head of the pancreas and the papilla of Vater in an effort to determine the patency of the terminal pancreatic duct system. In two cases the main pancreatic duct was found to be abnormal. In one of these cases the main pancreatic duct in the duodenal musculature was atresic. In the second case the main pancreatic duct was narrowed in the papilla of Vater. In both there was associated atresia of many interlobular ducts of the pancreas. In six cases the main pancreatic duct was patent, but many of the interlobular and intralobular ducts showed atresia. The authors state that the role of maldevelopment of both the large and the small components of the pancreatic duct system in fibrocystic disease of the pancreas can best be ascertained by careful examination of the pancreas and its ducts by serial section techniques.

Signet-Ring Cell Carcinoma of the Urinary Bladder.

O. SAPHIR (*Am. J. Path.*, March-April, 1955) states that signet-ring cell tumours, usually primary carcinomata of the gastrointestinal tract, may occur also as primary carcinomata of the urinary bladder. They are diffusely infiltrating lesions which occlude the ureteral orifices apparently early in their course, causing destructive pyelonephritis. Because of early invasion of the submucosal loose tissue and lateral spread, they are diagnosed late in the disease. Microscopically, they are mucin-secreting adenocarcinomata with a vast predominance of epithelial cells which resemble signet rings because of their mucous globules and which, isolated or in small groups, comparable to a phlegmonous inflammation, invade the entire wall of the bladder. Glandular structures may still be recognizable, but sometimes are difficult to find. Neighbouring structures may be invaded, but metastases are apparently rare, probably because of the short course of the disease, which terminates in uræmia.

Involvement of Internal Mammary Lymph Nodes in Breast Carcinoma.

J. P. WYATT, E. D. SUGARBAKER AND M. F. STANTON (*Am. J. Path.*, January-February, 1955) found that of 60 cases of primary cancer of the female breast, secondary growths were found in the internal mammary lymph nodes in 19; in seven these nodes alone showed metastatic tumour deposits. They state that this relatively high incidence of internal mammary nodal involvement reaffirms and emphasizes the importance of the anatomical and functional role of this lymphatic pathway from the breast. The primary cancer was located in the medial half of the breast in 13 instances and was subareolar in 14 examples. From these two sites alone metastatic tumour within the internal mammary nodes was found in 15 cases. This tumour-spread along the internal mammary pathway from malignant epithelial growths of the mesial half of the breast is, as far as ultimate biological behaviour is concerned, probably of greater importance than spread along the axillary channels.

Thyroid Carcinoma and Other Thyroid Diseases in Identical Twins.

D. W. ROBINSON AND T. G. ORR (*Arch. Surg.*, June, 1955) have studied three pairs of identical twins at the University of Kansas Medical Centre. The twins had three types of thyroid disease—carcinoma, non-toxic nodular goitre with cretinism, and exophthalmic goitre. They were all operated upon for their thyroid diseases. There have been no deaths. Twenty months have elapsed since the operations for carcinoma, with no evidence of recurrence. The twins with non-toxic nodular goitres and cretinism could not be traced. Six years after operation the twins with exophthalmic goitre were in good health and developing normally. The authors have not found a single report of carcinoma of the thyroid in identical twins in medical literature. They state that it is possible that such reports may be buried in reports of carcinoma of the thyroid in general and have not been found. If disease of the thyroid develops in one of identical twins, it may be expected to develop in the other at the same or some future time. If one identical twin develops carcinoma of the thyroid, the authors believe that there is justification for exploration of the thyroid of the other twin, even if clinical evidence of disease is not present. If evidence of nodular goitre is found, subtotal thyroidectomy is indicated, even if carcinoma has not been developed.

Pathology of Cerebral Palsy.

A. TOWBIN (*Arch. Path.*, April, 1955) states that cerebral palsy refers to motor disturbances which are mainly pyramidal or extrapyramidal in nature. The responsible lesions in the brain vary in origin; all are incurred during intrauterine or early infantile life. In the analysis of the cases in the present study, three pathological types were evident. In the first type the lesion was due to a developmental arrest of the brain. In the second type the cerebral lesion, destructive in nature, was the result of an antecedent systemic disorder present in fœtal or infantile life. In the third type the encephaloclastic lesion represented an intrinsically local intracranial disorder. The present report deals with the first type—cerebral palsy due to hereditary and induced developmental cerebral defects. Most developmental anomalies of the brain are induced; these defects represent the imprint left on the nervous system by exposure of the early fœtus to maternal infectious disease, irradiation or other noxious gestational influences. Developmental faults of the brain were associated with clinical manifestations of cerebral palsy in six cases of the series studied. In the severest cases, in an eight-year-old child displaying profound motor disturbances and mental deficiency, the brain at autopsy had the architectural features of that of a five-month fœtus. In addition to microcephaly portrayed grossly, histological evidence of developmental arrest was evident. In cases of less severe involvement, the brain showed localized anomalous development of the motor cortex. In general, the degree of motor disturbance displayed by the patients during life was proportional to the extent of developmental arrest observed in the brain at autopsy. The findings in this group, constituting approximately one-fourth of the cases of cerebral palsy in which the patient came to autopsy during the five-year period of this study, indicated the importance of faulty organogenesis as a cause of cerebral palsy.

Survival in Cases of Breast Cancer.

M. B. BLACK, S. R. OPLER AND F. D. SPEER (*Surg., Gynec. & Obst.*, May, 1955) have studied breast cancer patients in relation to the microscopic structure of the primary tumour and the regional lymph nodes. They state that the data would indicate that excellent survival rates are encountered when the cases are characterized by highly differentiated primary tumours, lymphoid infiltrate in the primary tumour and sinus histiocytic reactions of the regional lymph nodes. In those cases lacking such features a very low rate of five-year survivals exists. These relationships were obtained without regard to the age of the patient or presence or absence of axillary node metastases. The findings are consistent with the hypothesis that the lethal capacity of breast carcinoma varies as a direct function of the growth potential of the primary tumour as reflected in the nuclear structure and inversely as a function of tumour-retarding factors of the host visualized as sinus histiocytosis of the regional lymph nodes and lymphoid infiltrate in the primary tumour.

MORPHOLOGY.

Human Premaxilla and Maxilla.

W. M. SHEPHERD AND M. D. MCCARTHY (*Anat. Rec.*, January, 1955) state that there is considerable uncertainty in standard references of anatomy regarding the status and homology of the premaxilla and present evidence which purports to show that the wedge-shaped bone which carries the incisor teeth in man should be considered a separate entity homologous to the premaxilla found in mammals. They state that the premaxilla in man is homologous to that of other mammals with respect to ossification, position, conformation, function and bounding sutures, with the

exception of the facial portion of the incisive suture. The presence or absence of the facial portion of the suture, however, is actually a variable characteristic both in man and in the gorilla and should not be taken as proof of the non-homology of the premaxilla. Older concepts do not offer accurate explanations of the reason for the lack of maxillary-premaxillary suture on the facial aspect. The process of maxillary development on the facial aspect is one involving the fusion of the premaxillæ with the maxillæ proper, followed by erosion of the bodies of the premaxillæ and subsequent replacement of the bodies by trabeculæ arising from the maxillæ proper. The authors' conclusions were based on the study of 20 human embryos and fœtuses.

Selective Staining of Cupulæ and Otolithic and Tectorial Membranes of the Inner Ear.

G. B. WISLOCKI AND A. J. LADMAN (*J. Anat.*, January, 1955) give a complete account of the histochemical staining of the cupulæ and otolithic and tectorial membranes of the inner ear and discuss the possible significance of the results. They state that these structures have similar histological and histochemical properties; they contain a substance of a protein nature which is characterized by certain selective staining reactions relating them to several neural structures which exhibit similar staining properties—namely, the ciliary zonula, the secretion of the subcommissural organ of the epithalamus, Reissner's fibre and the Herring substance of the neurohypophysis. These structures are more closely allied to one another with respect to their staining properties than to other substances of the body (for example, elastic tissue, mucus), from which they can be shown to differ in one or more important ways. With regard to function, there is no apparent similarity between the structures; the several otic membranes in question and the ocular zonula are believed to exercise mechanical functions and the Herring material to bear a relationship to neurosecretory processes, while the functions of the subcommissural organ and of Reissner's fibre are unknown.

Relation of Nucleus to Nissl Material.

H. A. LINDSAY AND M. L. BARR (*J. Anat.*, January, 1955) report evidence in support of the view that the nucleolus participates in some way in the synthesis of Nissl material. They studied the behaviour of the nucleolus, sex chromatin and accessory body of Cajal during depletion and restoration of the Nissl material in neurons of the cat's hypoglossal nucleus. Changes in the nucleolus were followed in preparations stained with methyl green-pyronin, since the nucleolus stains with pyronin because of its content of desoxyribose nucleic acid. The sex chromatin also contains desoxyribose nucleic acid. Reduced silver methods are required to demonstrate the accessory body of Cajal. Swelling and vacuolation of the nucleolus occur during the period of most active restoration of the Nissl material. These changes are regarded as a morphological indication of increased activity on the part of the nucleolus. It is concluded that the nucleolus participates in the synthesis of the ribose nucleoproteins of the Nissl material. The sex chromatin of many neurons moves from the nucleolus toward the nuclear membrane during depletion and restoration of the Nissl material. There is a slight increase in the size of the sex chromatin during the same period. These observations are of interest since the sex chromatin appears to represent heterochromatic regions of the sex chrososomes, and since there is evidence from other sources that heterochromatic chromosome regions participate in nucleocytoplasmic interactions of a synthetic nature. The accessory body of Cajal, as seen in protargol preparations, decreases in size in chromatolytic neurons, but there is no obvious change in its position in the nucleus. So far as the authors are aware, the nature of the accessory body and whatever function it may have in the physiology of the cell are unknown. They state that it is important to distinguish clearly between the sex chromatin and other components of the nucleus, such as the basophile clots of Levi and the accessory body of Cajal.

Origin and Development of Sensory Ganglia of Cranial Nerves.

G. HALLEY (*J. Anat.*, April, 1955) traces the establishment of the sensory ganglia of the cranial nerves of the cat from the cranial neural crest and contributions of cells from placodal thickenings of the general ectodermal surface of the head. The cranial neural crest of the cat arises as three distinct masses—the trigeminal, the acoustico-facial and the vago - glossopharyngeal crest. The anterior portion of the trigeminal crest dissociates as mesectoderm, while the posterior portion remains relatively compact and forms the *Anlage* of the trigeminal ganglion. The ectoderm overlying the trigeminal crest becomes placodally active. Nodules and strands of epithelial cells detach from the epidermis and become incorporated with the trigeminal ganglion. The acousticofacial crest extends as a solid column of cells into the hyoid arch. Subsequently many of the crest cells in the epibranchial region degenerate, and the geniculate ganglion appears to arise in large part from an epibranchial placode. The auditory ganglion arises, at least in part if not entirely, from the epithelium of the auditory vesicle. The vago-glossopharyngeal crest differentiates into separate glossopharyngeal and vagal portions. Cells become detached from the distal ends of both vagal and glossopharyngeal crests and appear to contribute to the tissue of the more posterior branchial arches. The glossopharyngeal neural crest separates into superior and petrosal parts, and the petrosal portion fuses with an epithelial mass derived from the epibranchial ectoderm of arch III to form the petrosal ganglion. The vagal neural crest forms separate jugular and nodose portions. The nodose neural crest fuses with the epibranchial ectoderm of the dorso-caudal border of the cervical sinus, and the nodose ganglion arises at the site of this fusion. This epibranchial ectoderm is the placode of the vagus nerve, and represents the fused epibranchial placodes of the more caudal pharyngeal arches. Later, the placode of the vagus becomes submerged beneath the surface ectoderm and soon separates from it as a small vesicle. This vesicle eventually loses contact with the nodose ganglion but remains attached to the dorsal side of the third pharyngeal pouch.

Superior Vena Cava Anomaly.

S. A. HAUSMAN (*Anat. Rec.*, January, 1955) records an abnormality in a cat in which veins pass anterior to the heart. The failure of the left pre-cardinal vein to anastomose with the right in the development of the single superior *vena cava* leaves two prominent veins, left and right pre-cardinals of the embryo, which enter the heart separately, to become the functional adult veins.

Incorporation of Radioactive Isotopes in Mouse Tissues.

A. GLUCKSMANN, A. HOWARD AND S. R. PELC (*J. Anat.*, January, 1955) studied in mice the processes of differentiation and secretion in various organs, including the maturation of spermatozoa, by means of autoradiographs, using a radioactive isotope for "labelling" the cells and secretions to be studied. A solution of a protein carrying the isotope was injected into the peritoneum and on being absorbed and circulated was "taken up" by certain constituents in the organs to be studied. These were sectioned at 5μ, and autoradiographs were prepared by placing a thin photographic film in close contact with the mounted histological section and exposed to the radiation of the isotope. This technique allows the section and photographic film to be viewed simultaneously. Observations were made on unstained preparations with the phase-contrast microscope or on preparations stained with hæmatoxylin or carmine. The authors state that in the testis the isotope is found in the nuclei of spermatogonia and spermatocytes, and is retained during maturation. Timing of spermatogenesis based on the movement of the isotope leads to a figure of twenty-six days. In the epididymis the isotope appears at first in the cytoplasm of the epithelial cells and is later secreted on to the lumina. From the eighteenth day onwards positive autoradiographic findings in the lumina are associated with collections of "labelled" sperms. The seminal vesicles show a very strong uptake of isotope at first in the luminæ of the closely folded fundus region and later in the larger lumina of the central and urethral region. The uptake in the cells of the different parts of the gland is the same per cell, and the difference in the intensity of the autoradiograph over the secretion in different parts of the gland at different times can be related to the local ratio of the number of epithelial cells to the volume of the lumen and to the discharge of the secretion in the direction of the urethra.

Congresses.

THE AUSTRALIAN AND NEW ZEALAND ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE.

THE thirty-first meeting of the Australian and New Zealand Association for the Advancement of Science was held at Melbourne from August 17 to 24, 1955, under the presidency of PROFESSOR R. V. D. R. WOOLLEY, O.B.E., M.Sc., M.A., Ph.D., Sc.D., F.R.S.

THE SECTIONS.

The Sections represented were: A, Astronomy, Mathematics and Physics (including Optometry); B, Chemistry; C, Geology; D, Zoology; E, History; F, Anthropology; G, Economics, Statistics and Social Science; H, Engineering and Architecture; I, Microbiology, Epidemiology and Preventive Medicine (including Nutrition Subsection); J, Education, Psychology and Philosophy; K, Agriculture and Forestry; L, Veterinary Science; M, Botany; N, Physiology and Biochemistry; O, Pharmaceutical Science; P, Geography.

RECEPTIONS.

On Wednesday, August 17, His Excellency General Sir Dallas Brooks, Governor of Victoria, and Lady Brooks entertained senior office-bearers and distinguished visitors at a late afternoon reception. The presidential reception was held on the same day at Union House, University. On Monday, August 22, the Premier of Victoria, the Honourable H. E. Bolte, M.L.A., entertained office-bearers, their wives, distinguished visitors and interstate members in the Royale Ballroom, Exhibition Buildings, Carlton.

INAUGURAL MEETING AND PRESIDENTIAL ADDRESS.

The inaugural meeting was held in the Melbourne Town Hall on the evening of Wednesday, August 17, in the presence of His Excellency General Sir Dallas Brooks and Lady Brooks. The newly elected President, PROFESSOR R. V. D. R. WOOLLEY, delivered his presidential address entitled "Astronomy and Cosmology".

PUBLIC MEETINGS.

On the evening of Sunday, August 21, a forum entitled "Will Science Explain the Nature of Life?" was held in the Main Hall of the National Museum of Victoria. The chairman was SIR IAN CLUNIES-ROSS, Chairman of the Commonwealth Scientific and Industrial Research Organization, and the speakers were PROFESSOR A. A. ABBIE, of the University of Adelaide, DR. J. R. SMYTHIES, of the Australian National University, and DR. R. C. JOHNSON, Master, Queen's College, Melbourne.

A public discussion on "Benefits and Problems of the Atomic Age" was held on the evening of Tuesday, August 23, under the chairmanship of PROFESSOR L. H. MARTIN, of the University of Melbourne. Leaders of the discussion were PROFESSOR E. W. TITTERTON (Research School of Physical Sciences, Australian National University) and PROFESSOR D. G. CATCHESIDE (Department of Genetics, University of Adelaide).

VISITS TO SCIENTIFIC INSTITUTES AND HOSPITALS.

Members of Sections I and N attended a demonstration of research work at the Walter and Eliza Hall Institute, Royal Melbourne Hospital, on Thursday evening, August 18. Demonstrations were designed primarily to allow visitors to see the techniques currently being used rather than to provide "set pieces", and were as follows:

Methods of Production and Titration of Influenza Virus.—Dr. Margaret Edney.

Tumour Experiments in Mice.—Dr. D. Metcalf. (i) Technique of inoculation of foreign tissue into embryo mice. This is used to induce acquired tolerance to the foreign tissue as originally described by Medawar. This makes it possible to transplant mouse tumours to a foreign strain. (ii) Use of baby mice to demonstrate lymphocyte stimulating factor in chronic lymphatic leuchæmic plasma.

Recombination of Influenza Virus Strains.—Miss Patricia E. Lind. By mixed culture of two distinguishable viruses in deembryonated eggs recombinant forms can be produced. These carry some of the characters of each of the two "parents".

Tissue Culture.—Dr. E. L. French. Techniques were demonstrated in which were used human ciliated nasal epithelium and lymph node, monkey kidney, and chick embryo heart muscle. Lesions in monkey kidney due to aging or addition of normal human serum were shown.

Fluorescent Antibody.—Dr. J. O'Dea, who made two demonstrations: (*a*) synthesis of fluorescein isocyanate and the coupling of this material to antibody; (*b*) the detection of influenza virus in tissue using fluorescent antibody as an histological reagent.

Dark-Ground Microscopy of Filamentous Influenza.—Sir Macfarlane Burnet. Only the filamentous forms can be seen. They are damaged by a variety of surface active agents.

The Clinical Problem of Cystinuria.—Dr. R. K. Doig, who showed patients with excess of cystine in the urine presenting a history of recurrent stone in the kidney. This has been investigated biochemically and genetically in two families. Satisfactory management has resulted in reduction of the size of stones in two patients.

Purification of Iufluenza Virus.—Mr. G. L. Ada. The procedure utilizes the biological specificity of the virus enzyme and the physical properties of the virus particle.

Influenza Virus Nucleic Acid.—Paper chromatographic analysis of the purine and pyrimidine derivatives in influenza virus nucleic acid.

Freeze-Drying of Microorganisms Without Dry Ice.—Mr. H. Holden. The organisms in ampoules are kept below −10° C. in an ice-brine bath. The water vapour is removed from the system with calcium carbide which is readily available commercially.

Preparation of 2-Carboxy-Pyrrole from Mucoproteins.—Dr. A. Gottschalk, who showed chemical procedures involved in the preparation, isolation and identification of 2-carboxy-pyrrole from pure mucoproteins; 2-carboxy-pyrrole is derived from sialic acid, the component split off from mucoproteins by the influenza virus enzyme.

Electron Microscopy of Influenza Virus.—Dr. Heather Donald. (*a*) Specimen preparation, (*b*) shadowcasting, (*c*) examination in the electron microscope.

Members of Section I were invited to inspect the Royal Park Receiving House, Department of Mental Hygiene, and, together with members of Sections L, N and O, visited the Commonwealth Serum Laboratories, Parkville, on Wednesday, August 24.

PUBLIC LECTURES.

Artificial Rainfall.

On the evening of Thursday, August 18, a public lecture entitled "The Artificial Modification of Rainfall" was given by DR. E. G. BOWEN in the Main Hall of the National Museum of Victoria.

Preventive Medicine, Past and Future.

In his address given in the Melbourne Town Hall on Friday, August 19, SIR MACFARLANE BURNET said that the enormous increase in cigarette smoking was the most important cause in a quite frightening increase in lung cancer. He said that everything suggested that it took something like ten to twenty years before heavy smoking caused an increase in lung cancer, and, judging by current trend in figures and the still increasing consumption of cigarettes, the incidence of lung cancer would go on rising steadily for at least another twenty years. There were two reasonable approaches to what could be done about cigarettes and lung cancer. The facts should be known by the young. The smoker should make his own decision in the light of the information. The speaker saw no reason at all why a man who found pleasure in smoking should not decide that he was willing to pay for his enjoyment by a statistically certain, but individually uncertain, shortening of his life by five years. There was a definite obligation on medical men and others to dissuade the young from starting. A realistic approach was to establish by research what components in cigarette smoke were responsible for producing lung cancer in man, and to devise means of reducing the components to an acceptable level. The increase in lung cancer was most marked in Europe and the United States, although in Australia, a country still with a relatively low mortality rate, it had been increasing rapidly since 1920. Within the previous five years lung cancer had become a more important cause of death than tuberculosis in Australia, England and America.

Sir Macfarlane Burnet said that, while twentieth century preventive medicine had had great success, there were three other causes of death which showed clear upward trends. They were coronary disease, leuchæmia and death by violence. Coronary disease was carrying off an increasing

number of men in their forties and fifties. Its association with cigarette smoking was unmistakable in a survey by British medical statisticians, but it was not wholly to be blamed on cigarettes; it was in some way related to the stress of modern living. The important factor was the patient's inherited constitution.

Leuchæmia might become increasingly important with the development of atomic energy, whether for war or peace. It was the only chronic result of exposure to the bombs of Hiroshima and Nagasaki that had been definitely established.

Deaths by violence were occasioned largely by motor vehicles, about which medical men could do little but prevent people from dying. Lung cancer, coronary disease, leuchæmia and accidental violence were probably in principle preventible, but their control would be far more difficult than that of infectious diseases like tuberculosis and diphtheria. Infectious diseases in Western countries were becoming less important as the cause of death. Since 1946 deaths from tuberculosis had dropped so rapidly that the disease might be extinct in twenty years.

Discussing poliomyelitis, Sir Macfarlane Burnet said that it was the only infectious disease to show a rise in incidence and mortality in the previous fifty years. Dealing with the current promise of prevention through the use of the Salk vaccine, he said that for a vaccine to be efficient it must be able to protect that unfortunate fraction of less than 1% of children who, for one reason or another, would otherwise suffer the paralytic disease. That was the reason why in the American experiments in 1954 it had been necessary to test some hundreds of thousands of children to assess the efficiency of the Salk vaccine. Only about 115 children contracted typical poliomyelitis in the uninoculated group and 33 in the inoculated group. Each group comprised 200,000 children. It was thus of the utmost importance that there should be no risk whatever of doing harm by the vaccination procedure. As with other vaccines, science used the antipoliomyelitis vaccine to imitate Nature's process of immunization by an attack of the disease, but the case of poliomyelitis was a special one. On the whole, Nature did her job of immunization against poliomyelitis very efficiently, with only a small proportion of damaging infections. The poliomyelitis virus spread rather easily, almost as easily as the virus of measles, but in 99% or more of children it produced no obvious sign of its presence. An invisible epidemic could spread through a city or State with its presence marked only by the appearance of scattered and apparently unconnected cases of paralysis in the rare, unfortunate child. It was for this 1% that science was continuing its battle for an effective vaccine to give efficient and safe immunization against the disease.

CHURCH SERVICES.

On Sunday, August 21, a special combined interdenominational church service was held at St. Paul's Anglican Cathedral, where the preacher was the Reverend J. Davis McCaughey, Professor of New Testament Studies, Ormond College, Melbourne. A special service for delegates was held at the Independent (Congregational) Church. A special Mass was held at St. Patrick's Cathedral.

1957 CONGRESS.

It was agreed that the next meeting of the Australian and New Zealand Association for the Advancement of Science should be held at Dunedin, New Zealand, in January, 1957, the President-Elect to be Professor Sir Macfarlane Burnet.

SECTION D: ZOOLOGY.

Genetic Effects of Radiations.

D. G. CATCHESIDE (Adelaide) discussed the genetic effects of radiations. He said that there was an underlying relationship in the causation of genetic changes, induced in germ cells and expressed in descendants, and of injury, such as blood damage, tumours and leuchæmias, caused to the somatic tissues of an exposed individual. All involved destruction or loss of function of various constituents of cells. Non-genetic material destroyed might be replaced after a period of depression of metabolic activity. However, after such a shock the cell might be altered in its mode of differentiation, including rate of division, leading to neoplasms.

Professor Catcheside went on to say that the killing of cells was usually consequent upon injury to the chromosomes, either by producing "sticky" mitoses or by causing breaks in them proportional in number to the dosage received. Loss of acentric fragments and disorganization of mitosis by the production of sister union or interchange chromosome bridges led to the death of cells and of tissues. Tissues as a whole might show "recovery" through the replacement of the damaged and killed cells by uninjured or less injured cells.

Finally, the genes might be altered or minute deletions of parts of the chromosomes produced, the latter simulating gene mutations, often in a more extreme form. The number of such genetic changes was linearly proportional to dosage and independent of dose rate down to the lowest tested. They appeared to be strictly cumulative and showed no recovery towards the normal.

The radiation-induced changes as a whole were harmful. A population subjected to radiation hazards would have the induced changes added to the already considerable load of harmful genes that it carried. They would lead to a lowering of the average fitness of the population and also to an increase in the frequency of genetic death, with which the total mutation rate, spontaneous and induced, was in equilibrium in a stable population. Calculations of the effect on a population depended upon knowledge of the existing amount of genetically caused defect, the natural mutation rate in a generation and the dosage required to give an equal induced mutation rate. Evidence from flies and mice indicated that this doubling dose was about 100*r* if given to immature germ cells.

SECTION F: ANTHROPOLOGY.

Primitive Peoples.

In his presidential address PROFESSOR S. F. S. NADEL (Canberra) spoke on "Understanding Primitive Peoples". He said that the primary aim of anthropology had always been the understanding of primitive man, of the cultures he had created and of the types of society in which he lived and acted. "Understanding" here covered a number of things; but basically it meant discovering, in ways of acting and thinking widely different from our own and often puzzling to Western eyes, intelligible principles and rules. In a sense this was a task of translation, from the idiom of one civilization into that of another; and it could be pushed too far. Too ready or complete a "translation" might empty the primitive cultures of all that was peculiar to them. Yet conversely, the insistence on their unique and "untranslatable" nature would preclude any wider comparison and hence stultify the very notion of understanding. But this kind of dilemma was not unfamiliar in the other social sciences.

There was sense in asking the question: "How do we begin to understand primitive peoples?" Modern anthropology would reply: through field work—through living with the people they studied, through observing their behaviour and becoming steeped in their mode of life. Professor Nadel said that this was only half the answer. Certain practical barriers, such as language and the difficulty of establishing *rapport*, had to be overcome by the adequate training and selection of the field worker. The dangers of subjectivity and impressionism had to be controlled by precise techniques of sampling, interviewing, and recording of evidence. But certain more fundamental difficulties remained. Observation, however intimate and apparently complete, was futile unless based on some kind of blueprint; successful practical work in the field presupposed a theoretical framework capable of guiding and foreshadowing lines of inquiry. The continuing expansion of anthropological knowledge precluded any very rigid guide of such a kind: discoveries of new, unforeseen facts would still happen. But modern anthropology was growing steadily more independent of accidental discoveries and moving towards the more precise formulation of problems to be solved and theories to be tested. All this meant a training of the young anthropologist, infinitely more exacting and complicated than that in use only twenty years earlier.

It was part of the heritage of anthropology that its scope should be essentially synoptic, concerned with the analysis (or "understanding") of total societies. This posed the problem of specialization. It was negligible at the level of truly primitive groups, with simple technology and undeveloped law or political organization. But in dealing with more complex societies or societies affected by modern changes, it became doubtful if the anthropologist could continue to play the part of an all-round expert, versed in social organization, economics, law, politics, and so on. The answer seemed to lie in team work, though this, too, had its problems, of profitable collaboration and the most fruitful division of labour.

Professor Nadel went on to say that today anthropologists had embarked on the study of modern societies, thus encroaching on the fields conventionally assigned to sociologists, historians or political scientists. If the anthropologist had anything of his own to contribute, it lay in his

sensitivity to the small-scale features of social life, which only living with the people and day-to-day observation could make accessible. It was no accident that most of the studies in question were concerned with local communities or with even narrower units, family and kin. But there was a further contribution the anthropologist could make; for, trained to think in terms of widely varying societies on diverse levels of civilization, he brought to his observations the more searching comparative viewpoint.

That such a viewpoint existed was the result of the numerous monographic studies already possessed, covering a wide section of the inhabited globe. That knowledge still needed to grow much larger. Equally, it needed synthesizing. For it was only through explicitly comparative studies based on all the available data and systematized in a unified theory that it would be possible ultimately to understand, not only this or that society, but human society at large, in all its variations. Oddly enough, the men needed for this task were slow in coming forward. The pressing need for more and more field studies was partly responsible; but the inherent attraction of work in the field undoubtedly also played a part. Perhaps hope should be entertained for a new breed of anthropologists ready to bid farewell to the romantic age of exploration and to embrace instead the new era of scientific consolidation.

A Report on Blood Group Genetical Surveys in Eastern Asia, Indonesia, Melanesia, Micronesia, Polynesia and Australia in the Study of Man.

R. T. SIMMONS (Melbourne) said that blood groups determined in the laboratory were the observed expression of particular genes inherited from a remote past. Instead of scientists visiting the natives and working in the field, technique developed in Melbourne utilized small bottles of blood preservative and flasks in which the blood samples were flown to Melbourne in ice.

Earliest blood group studies in man were made with the use of the A-B-O groups alone; next came A-B-O, M-N and P. Discovery of the Rh blood groups followed by other blood group systems in quick succession, such as Lewis, Duffy, Kell, Lutheran, Kidd *et cetera*, crowded into ten years most spectacular advances in knowledge. The reagents used in blood grouping—the antisera—were found in human blood as the result of incompatible blood transfusions, or in cases of iso-immunization in pregnancy.

Mr. Simmons said that Melbourne workers had presented gene frequencies for Eastern Asians and Indonesians, including Ainu, Japanese, Chinese, Thais, Chenchu (India), Philipinos, Indonesians from Java and twenty other islands and groups in Borneo. The Melanesian peoples tested included negritos of Dutch New Guinea, coastal Papuans, Central Highlanders of New Guinea, Bainings and West Nakanai of New Britain, Admiralty Islanders, New Hebrideans, Fijians and natives of New Caledonia and Loyalty and Pine Islands; in Micronesia: Palauans, Trukese, Marshallese, Kapingas and Gilbertese. There had been several surveys on Australian aborigines, the most recent being on nearly 2000 natives in Western Australia. In Polynesia, the Maories of New Zealand and Cook Islanders had been investigated. Mr. Simmons mentioned gene frequency patterns in each geographical area, and the limited conclusions which could be drawn to date. For example, there was no serological evidence that any race closely related to the African Negro ever entered the Pacific. Polynesians had a close blood genetic relationship with American Indians which was not generally evident with Melanesians, Micronesians or Indonesians. Mr. Simmons discussed data on the Polynesian problem at some length.

SECTION I: MICROBIOLOGY, EPIDEMIOLOGY AND PREVENTIVE MEDICINE.

Living Molecules: A Review of Recent Advances in Our Understanding of the Nature of Viruses.

In his presidential address to Section I, R. J. BEST (Adelaide) said that about 1933 the popular conception of a virus was of a submicroscopic living organism, perhaps like a miniature bacterium. About this time chemists applied their ideas and techniques to a study of plant viruses and soon had isolated a number of them and found them to be nucleoproteins, with molecular weights of the order of millions. Different virus types were found to differ in the proportion of nucleic acid they contained, and different strains of one virus type differed in the organization of the subunits of which they were composed, and sometimes in the relative proportion of constituent amino acids. Current investigation suggested that there was considerable scope for variation in both the protein and nucleic acid moieties of the molecule and that both might be involved in determining specificity.

Of the bacterial and animal viruses which had been sufficiently investigated some seemed to be similar to plant viruses in respect of chemical composition, deoxyribonucleic acid being characteristic of bacterial viruses and ribonucleic acid of plant viruses. However, some of the larger animal viruses seemed to be more complex, suggesting that the viruses might be a heterogeneous group of entities. Interpretation was also made more difficult by lack of knowledge of the extent to which portions of the host cell remained attached to the minimal essential infective unit.

Dr. Best said that in studies of the interaction between virus and host the leading questions were: "To what extent did the host participate in the reactions into which the virus entered?" and "How did viruses develop and multiply in their hosts?" Workers with bacteriophage had concluded that the protein portion of a particle was responsible for attachment to and invasion of a host, and that it was the nucleic acid portion of the virus which entered the cell and caused the replication of more of itself. Dr. Best asked what was the significance of the "dark phase" noticed immediately after infection of the hosts by bacterial, animal and plant viruses. Visconti and Delbrück's theory, proposed to explain recombination in bacterial viruses, could not yet be tested for plant viruses, but at Adelaide they had obtained evidence that two strains of one plant virus reacted *in vivo* to form new strains which differed from both parents but combined in themselves some of the characters of each. (This was illustrated by "Kodachrome" transparencies.)

Dr. Best went on to say that it would seem that at some stage during the replication process an exchange of genetic material took place between particles of different strains, and that this material was part of the nucleo-protein core of the virus. It seemed likely that the genetic memory of a virus was in its nucleic acid, that the protein portion was essential for infection and invasion and that the nucleic acid, alone or accompanied by some protein, entered the genetic mechanisms of the invaded cell and used existing enzymes to direct the synthesis of more of itself. The level at which the genetic mechanism was entered was not known and might be different for different kinds of virus.

The manner in which the nucleic acid and protein of the molecules were linked, the morphology of simple virus particles, must be important in the foregoing connexion and there were several recent contributions which threw light on that point. According to one line of work tobacco mosaic virus appeared to consist of a series of protein disks, with a hole through the middle, strung together by a continuous central thread of nucleic acid. There was also evidence for a helical structure for nucleic acids and nucleo-proteins and for at least one virus (T.M.V.). It could well be that in the fibrous viruses the nucleic acid acted like a helical wick in a helical candle where the wax of the candle represented protein. Dr. Best asked how the units responsible for hereditary characters fitted into this structure. Did turnip yellow-mosaic with its core of nucleic acid apparently completely encased in a protein shell fit into this scheme or did it represent a different morphological group?

Poliomyelitis.

Opening a symposium on poliomyelitis, H. MCLORINAN (Melbourne) spoke on "Paralysis in Poliomyelitis". He said that there was strong evidence to support the belief that certain non-specific factors determined the frequency of paralysis in poliomyelitis. The evidence in favour of predisposing or provoking effects of (*a*) excessive muscle fatigue and trauma, (*b*) certain immunizing injections, (*c*) the operation of tonsillectomy, and (*d*) pregnancy might be regarded as convincing. Other factors which had been considered were excessive mental strain, dietary deficiencies, and conditions producing increased metabolism.

The application of the knowledge of such predisposing factors of paralysis might be extended to the study of such diseases as disseminated sclerosis, infective polyneuritis, Bell's palsy and other peripheral neuritic conditions.

In conclusion, Dr. McLorinan said that the management of the acute case of poliomyelitis by complete mental and physical rest aided by judicious sedation had met with a limited amount of success in the prevention of spread of the paralysis.

Laboratory Studies on Poliomyelitis in Victoria.

A. A. FERRIS (Melbourne) reviewed the epidemic and endemic poliomyelitis virus strains in Victoria since 1949. This information was provided in the main by virus isolations, but was amplified by certain group studies of antibody response during epidemics. Dr. Ferris noted that, as was the case elsewhere in the world, type I (Brunhilde) virus had been the predominant strain.

He correlated these findings with age group studies of antibodies to the three poliomyelitis viruses in Victoria. One study had been carried out at the Commonwealth Serum Laboratories in Melbourne, and a current study was in progress at the Epidemiological Research Unit at Fairfield. For the latter study Dr. Ferris said that a controlled collection of sera had been undertaken, over a specified period of time, with at least 30 sera in each age group from one to thirty years, and lesser numbers in groups up to the age of seventy-five years. Such studies of the process of natural immunization in the community were especially relevant at the present time when production of a poliomyelitis vaccine for mass immunization was being undertaken.

Variants of Poliomyelitis Virus.

N. F. STANLEY (Sydney) said that his paper was confined to variations in the paralytic, antigenic and cytopathogenic behaviour of types I, II and III poliomyelitis viruses. The methods used to derive strains with reduced paralytic ability for monkeys were reviewed, with special reference to the observations of Cox and Koprowski, Sabin, Li and Schaeffer, and Krech. Dr. Stanley described the development of variants following intracerebral inoculation of an Australian strain of mice.

A new approach to the problem was indicated by the demonstration of three paralytic maxima following intracerebral inoculation of infected cord suspensions in mice. By a combination of differential ultracentrifugation and agar diffusion (Polson's method) it was shown that the particles comprising the three paralytic maxima were approximately 30, 24 and 19·2 millimicrons in diameter respectively. Furthermore, it was shown that the largest particles (30 millimicrons) were non-paralytic for monkeys intracerebrally, but the smaller ones were paralytic following intracerebral inoculation. A freshly isolated strain of type II poliomyelitis virus from a patient with paralysis gave no evidence of the presence of the large non-paralytic 30 millimicron particle. Dr. Stanley suggested that the three particle types probably occurred in Nature and that the severity of an epidemic or the ability to cause paralysis in an individual could probably be related to the predominance of one size particle or another.

In discussing vaccination in attempts to prevent poliomyelitis epidemics, Dr. Stanley indicated that four possibilities or combinations of them now existed. The first was the formalinized paralytic or Salk type, which was given intramuscularly or subcutaneously; the second was the formalinized non-paralytic, given by the same routes; the third, the controlled, attenuated, living virus given intradermally; and the fourth, a disseminated attenuated living virus given orally. Of these, the first was the most artificial and the last the most natural. If it was considered desirable to administer a killed vaccine to children in Australia, Dr. Stanley recommended that the highly paralytic strains at present being used be replaced by the non-paralytic strains now available, provided they were antigenic. Quite a few of the living attenuated strains Dr. Stanley spoke about had already been used in small-scale human experiments and had proved to be uniformly successful in respect to immunity and safety. Any one of them might eventually meet the requirements for its incorporation in a living attenuated vaccine.

It had yet to be proved that any protection derived from administration of killed virus approached in effectiveness that derived from the natural infection. All the problems discussed obviously demanded an urgent study of the natural process of immunization in poliomyelitis—processes about which very little was known, although they appeared to be highly effective. Furthermore, they demanded continued investigation of variation and virulence, the results of which should determine to a considerable extent the success of attempts to prevent disease.

Requirements for a Killed Poliomyelitis Vaccine.

E. V. KEOGH (Melbourne) very briefly summarized in table form pertinent data from the Francis report, further details of which may be found in an article by Francis and Korns in *The American Journal of the Medical Sciences*, 1950, Volume 229, page 603, and Francis *et alii* in *The American Journal of Public Health*, 1955, Volume 45, Number 5. Those results showed the antibody responses to the three types of poliomyelitis virus and the protection derived therefrom in the wide-scale experiment on children recently carried out in the United States of America. Dr. Keogh said that there were as yet no published data in scientific and medical journals on the paralysis in children resulting from administration of Cutter vaccine. That would probably be brought to light as the result of court procedures. Dr. Keogh thought that preparations of the Salk vaccine contained live virus, but that it was in sufficiently small amounts to be insignificant. The duration of immunity and how long the serum antibody remained at a high level in response to vaccination were not yet known. Dr. Keogh thought that the paralysis resulting from administration of certain batches of vaccine in the United States of America was the result of an accident, which was likely to happen with any similar preparation.

Influenza Virus as a Microcosm of General Biology.

In his address to Sections I and N, SIR MACFARLANE BURNET briefly outlined the research carried out on influenza by the Hall Institute during the last twenty years. Those studies, he said, had been at two different levels. The first was concerned with influenza as a human disease, its laboratory diagnosis, and problems of serology and immunology. Here, the most important contribution was the establishment of the chick embryo as the standard experimental host for the study of influenza viruses. The second level—the subject of his address—was concerned with the study of influenza virus for its intrinsic qualities rather than as an agent of human disease. Sir Macfarlane Burnet outlined the picture of influenza virus as developed during the previous ten years, mainly from a study of hæmagglutination.

The outstanding characteristics of a typical influenza virus were:

1. Infective particles have a definite morphology (spheres or filaments).
2. It is readily adapted to free growth in allantoic cells.
3. It agglutinates red cells by particles forming bridges.
4. The process of infection of influenza and probably all other animal viruses involves the following sequence: (a) specific adsorption to cell receptors, (b) the eclipse phase, (c) accumulation of virus products intracellularly, (d) liberation of new descendent virus.
5. In addition to the virus particles a soluble (small particle) substance produced as a result of infection can be defined by immunological tests—complement-fixing antigen. This is produced only as a result of infection—the corresponding antibody has no protective power.

It was on these phenomena that the picture of influenza virus was established.

Sir Macfarlane Burnet discussed (with illustrations) the characteristics of soma and genome. He indicated that adsorption was intimately related to enzymic action and that both were directed toward mucoprotein. The importance of destruction of enzymic activity with retention of adsorptive pattern was stressed. The use of receptor-destroying enzyme and a hint as to the chemistry of the process as defined by Dr. Gottschalk were described. "It is probable that the enzymatically active groups are incorporated in molecules of specific virus protein on the surface of the infective particles—and that the antigenic determinants which are responsible for the immunological behaviour of the virus are part of the same molecules."

When an influenza virus particle entered a cell it disappeared ("eclipse phase") and it was likely that the somatic components took no further part.

Evidence as to what was taking place had to be drawn essentially from experiments in which more than one virus particle entered the same cell. Depending on various circumstances, double infection might result in: (i) Interference—an inert particle could prevent multiplication of an active particle. (ii) Production of incomplete virus of limited or no further capacity for infection and multiplication. (iii) Multiplicity reactivation in which two particles, neither of which alone could multiply, could together produce viable (or incomplete) descendants. (iv) Recombination in which progeny were produced which showed characters derived from two different parental forms.

The main conclusions to be drawn from the analysis of these phenomena were: In the first place interference was interpreted as the blocking of a functioning cell unit by specific adsorption. There was evidence to suggest that these cell units started to multiply soon after effective contact was made—and rather speculative suggestions that they were of microsomal character—nucleic acid (RNA) and protein complexes—and that when they were stimulated to replicate by active virus they had the quality of soluble complement-fixing antigen. In the second place incomplete virus was probably virus with an inadequate content of genetic material—it was known to be deficient in nucleic

acid. Finally the incorporation of inheritable qualities from two parents either in the guise of multiplicity reactivation or as recombination was the most direct evidence for the existence of a common pool of replicating genetic components from which progeny were organized and withdrawn in essentially random fashion.

Sir Macfarlane Burnet described recent observations on three types of genetic interaction between influenza viruses. This involved a discussion of recombination with strains MEL and WSE. After a brief discussion of morphological and chemical factors, Sir Macfarlane Burnet concluded that probably those present would be able to see how a rather simple general picture of the virus was starting to emerge. This picture might be and probably was considerably too simple, but Sir Macfarlane Burnet felt confident that it represented the essential framework on which the definitive interpretation would be erected.

The virus particle was a shell of virus protein molecules united with 30% of lipid to form a surface rather similar to that of a red cell. Within the particle were nucleoprotein units which were the carriers of the genetic qualities and probably a variety of casually incorporated molecules.

Regarding the nucleoprotein (RNA + protein) as the genetic units, he would switch to genetic conventions to discuss them more closely. It was believed that there were two types corresponding to the *A* and *C* linkage groups, and that each virus particle contained a number perhaps between 5 and 50 of each sort. These units, which were called non-committally gene threads, must be self-replicating and also capable of controlling the synthesis to specific pattern of the specific virus protein needed for surface function of the infective particle. The gene threads were subject to mutation at any locus Aa Bb *et cetera*, being regarded as allelic forms.

Within the susceptible cell the entry of the virus gene threads initiated a process by which the synthetic mechanisms of the cell cytoplasm were diverted to the synthesis of virus protein and nucleic acid, the patterns for which were provided by the invading virus elements. A pool of replicating material developed in which there was a competition for survival amongst any gene threads with allelic differences. Where these allelic differences concerned virulence this competition was probably of vital importance.

When the pool was of sufficient concentration at the cell surface, surface active specific virus protein molecules could be regarded as interacting with cell surface components to segregate and enclose a portion of the surface pool. This budded off as a virus particle. It naturally included a considerable complement of host material.

From a mixed infection the progeny would present a complex variety of surface and genetic characters mostly very mixed—hence the heterozygotes and phenotypic mixtures of the first cycle fluids.

But it should be stressed that in the course of every virus multiplication from a single particle there arose a complex problem in population genetics. There was competition between gene threads carrying different alleles inside the cell and there was another competition for survival between the different types of infective particle produced. As a result, when a single heterozygous particle was introduced into a chick embryo, there was found at the end of incubation a population dominated by a single one of the various potential descendants of the original heterozygote. This selective survival was the key to the understanding of influenza virus genetics.

The Patterns of Macromolecules in Relation to Biological Specificity.

A symposium was held jointly by Sections D, M and N on Friday, August 19. The speakers were as follows: F. M. Burnet (Melbourne), Chairman, "The Significance of Macromolecular Pattern"; Phyllis M. Rountree (Sydney), "The Biological Specificity of Macromolecules in Bacteriophage Synthesis"; D. G. Catcheside (Adelaide), "The Gene: Its Nature and Function"; J. M. Rendel (Sydney), "To What Extent are all Organisms Built up of the Same Gene Units?"; D. O. Jordan (Adelaide), "The Structure of Nucleic Acids in Relation to Biological Specificity"; G. L. Ada (Melbourne), "Nucleic Acids of Viruses"; H. Lindley (Melbourne), "The Structure of Proteins in Relation to Biological Specificity"; A. Gottschalk (Melbourne), "The Specificity of Enzymes"; F. D. Collins (Canberra), "The Structure of Lipids in Relation to Biological Specificity"; A. J. Hodge (Melbourne), "The Patterns of Lipoprotein Structures as Revealed by the Electron Microscope".

Spread of Streptococcus Pyogenes in the Community.

MARGARET C. HOLMES (Melbourne) said that the distribution of serological types of *Streptococcus pyogenes* could be used to study the spread of streptococcal infection in the community. An analysis of strains isolated from patients admitted to Fairfield Hospital during the period 1950-1954 gave some indication of the pattern of spread in a large city.

More precise information could be obtained from detailed studies of small communities, and the results of such a study carried out over a period of thirty months in a large orphanage on the outskirts of London were used to discuss the way streptococci spread both in a semi-closed village community and within the family units which comprised it.

Evidence for Leptospiral Serotypes in Australia, New Zealand and the Territory of Papua-New Guinea.

J. S. WANNAN (Sydney) said that sources of information for the evidence presented were: (*a*) medical and veterinary publications of Australia and New Zealand; (*b*) annual reports and publications from various government departments of Australia and New Zealand; (*c*) personal communications from research workers; (*d*) unpublished laboratory records of the School of Public Health and Tropical Medicine, Sydney.

An outline was given of the methods used to determine: (*a*) the cultural evidence, (*b*) the serological evidence. A large table setting out the complete information collected had been prepared, and from this several small tables giving the relevant importance of various aspects were shown.

Up to 1953 only five leptospiral serotypes had been isolated and completely identified. Since then some further six had been determined, making a total at present of eleven serotypes. In addition to these, Mr. Wannan said that there was strong serological evidence for one other serotype. Antibodies to other serotypes had been demonstrated in animals, but the significance of these was at least doubtful at present. In this respect more extensive investigations of field rodents and other possible reservoirs might prove of value.

A Case of Nocardial Mycetoma of the Foot due to Nocardia Maduræ.

GALENA DEMENTJEV (Queensland) described the isolation of *Nocardia maduræ* in three instances within a period of two months from the white-yellow granules obtained from the pus of an actinomycotic lesion of two years' duration on the left instep of a twenty-six-year-old female patient from Jandowae, Queensland. The organism grew slowly in primary cultures by the use of special techniques; growth was obtained after five to seven days' incubation on different laboratory media. The organism was not acid-fast, grew in strictly aerobic conditions, did not produce acid from sugars, hydrolyzed starch, liquefied gelatin after six weeks and peptonized litmus milk after prolonged incubation. A pink to dark red pigment was produced irregularly. Colonies were very hard and adhered to the media and, in early development or in liquid media, had a pronounced filamentous edge. After four weeks' incubation, a papillate outgrowth was produced on the central portion of the colony. The organism was remarkably resistant to drying and was viable after a prolonged period in water. It was killed by heating to 60° C. for fifteen minutes, survived a ten-minute contact with a 1 in 500 solution of "Zephiran", but was killed in ten minutes by 70% alcohol and 5% phenol. The organism was resistant to 200 units per millilitre of penicillin and even grew in an aqueous solution of this strength. It was sensitive to 1·6 milligrammes per millilitre of streptomycin and 6·25 milligrammes per millilitre of "Terramycin". It did not show any remarkable sensitivity to "Aureomycin", "Chloromycetin", "Achromycin" or polymyxin.

Nocardia maduræ caused local nodular lesions after repeated subcutaneous injections into rabbits, rats and guinea-pigs. The organism had been recovered from the pus present in the nodules of infected rats. The arrangement of fungal filaments in experimentally produced excised nodules of rabbits had been studied in histological sections. No antibodies had been revealed in inoculated rabbits.

Cervical and Vaginal Smear Patterns in the Common Types of Puerperal and Abortional Infections.

HILDRED M. BUTLER (Melbourne) said that in puerperal and abortional infections cultural methods as a means of bacteriological diagnosis were inadequate for two reasons. Firstly, such methods were too slow, and secondly, they often failed to distinguish between the bacteria which were

the actual cause of a genital tract infection, and the bacteria which either were normal inhabitants of the vagina or were present as the result of contamination with fæcal material or infected urine.

Both these disabilities, the lack of speed and the failure to distinguish between the causative bacteria and the normal inhabitants or contaminants of the genital tract, largely disappeared if bacteriological diagnosis was based on the examination of stained smears made directly from the suspected infected area. In practice it was usually satisfactory to make the smears from high vaginal swabs in puerperal cases and from cervical swabs in cases of abortion.

Dr. Butler went on to say that this method of smear diagnosis was based on the observation that each particular type of infection had a characteristic smear picture or pattern.

Approximately 70% of the infections seen at the Royal Women's Hospital, Melbourne, were due to anaerobic bacteria: anaerobic streptococci, non-sporing anaerobic Gram-negative bacilli (*Bacteroides*) and *Cl. welchii*. The other 30%, the aerobic infections, were mostly due to *Strep. hæmolyticus* Group A, Group D streptococci, *Bact. coli* and staphylococci. In 90% of cases direct smears provided an accurate indication of the bacterial type or types causing the infection.

Dr. Butler showed and discussed smears typical of the various infections and paid particular attention to the differentiation of infection with fæcal bacteria from mere contamination with such bacteria.

Tuberculosis.

To open the symposium on tuberculosis, E. V. Keogh (Melbourne) spoke on "The Relation of Morbidity to Mortality in Tuberculosis". Dr. Keogh said that in the fifty years prior to 1946, tuberculosis mortality in Victoria had declined at a uniform rate. In that year, specific chemotherapy of tuberculosis was introduced. Subsequently, the rate of decline in mortality had markedly accelerated. There had been no decline in notifications of new cases. Evidence suggested that the new cases now reported were less severe than those formerly notified. Consideration of all the available evidence suggested that morbidity from tuberculosis was, in actual fact, declining.

Tuberculosis Death Rates Treated by Generation Method.

H. O. LANCASTER (Sydney) said that the death rates from tuberculosis still formed the best information on the importance of tuberculosis in the human population. In a time of falling death rates, quite false interpretations could be made if attention was fixed on the death rates at a point of time. The study by generations was of more interest biologically. It led to the view that death at the higher ages must usually proceed from long-standing infections. For comparison with tuberculosis, statistics of deaf-mutism, goitre and lung cancer were briefly mentioned. The generation method could be used for forecasting. It had relevance also to the interpretation of the results of Mantoux testing in tuberculosis and analogous tests in other diseases.

Allergy in Tuberculous Mice.

D. F. GRAY (Melbourne) discussed the mouse response to experimental tuberculosis. He said that previously the mouse response was believed to differ from that of other animals in several important respects: (*a*) unusually high resistance to infection, (*b*) failure to develop the typical cellular response of the classical tubercle, (*c*) failure to become allergic, and (*d*) failure to develop specific immunity. It was now recognized that mice did develop an effective immunity when injected with living or killed tubercle bacilli. The present paper dealt with their extreme susceptibility to intranasal infection compared with other routes of inoculation, with the nature and importance of their cellular response, and also with the development of allergy in relation to the progress of primary infection.

There was little reason to suppose that immunity in the mouse was based on mechanisms essentially different from those operating in other animal species.

The Present Status of Biology in Secondary and Tertiary Education.

Speakers in a symposium on the present status of biology in secondary and tertiary education were P. D. F. MURRAY (Sydney), "The Present Status of Biology in Tertiary Education"; F. F. FITRIDGE (Melbourne), "The Present Status of Biology in Victorian Secondary Education"; and G. R. MEYER (Sydney), "Some Results of a Survey of Biology Teaching Practice in N.S.W. Secondary Schools". This was a joint symposium for Sections I, J, M and N.

Myxomatosis.

F. N. RATCLIFFE (Canberra) reviewed myxomatosis in Australia from 1950 to 1955. He said that the early indication of the importance in Australia of mosquitoes as myxomatosis vectors had been confirmed. Only one other insect group—the Simuliidæ—had been positively incriminated, and they could be of local importance. Increased knowledge of the ecology and behaviour of certain mosquito species provided an explanation for some types of disease activity which at first seemed inexplicable.

The field performance of myxomatosis was primarily a reflection of the distribution and prevalence of certain species of mosquitoes. Each season since 1950 had had its own marked individual character; but the overall effect of myxomatosis—at any rate in the three eastern mainland States—had been an accumulating decrease in rabbit numbers (allowing for the interepizootic build-up).

Differences in mortality due to variations in the infection rate—due, in turn, to seasonal and local differences in vector abundance—had been far more obvious and important than the decrease in case mortality rate due to the appearance and establishment of attenuated strains of the virus; though this must have been a factor in determining the extent of interepizootic recovery in local rabbit populations.

Mr. Ratcliffe said that none of the five "myxomatosis seasons" to date had lacked good rains. A year with sufficient rain to encourage rabbit breeding, but not enough to maintain surface waters and vector populations, had yet to be experienced.

Myxomatosis had had a negligible or disappointing effect in Western Australia, western South Australia and Tasmania.

Unsolved problems included: (*a*) the identity of the vectors in certain areas; (*b*) reasons for the failure of the disease in some areas where conditions appeared to be favourable; and (*c*) the justification and value of artificial inoculation, once myxomatosis had become generally established and enzootic.

F. FENNER (Canberra) discussed "Changes in the Virulence of Strains of Myxoma Virus". He said that effective control of the numbers of an animal with the reproductive capacity of the rabbit by means of an infectious disease demanded the combination of ready transmission within a very high mortality rate. Myxoma virus, as it escaped into the Australian rabbit population in 1950, fulfilled both these requirements. Within a few years, however, field evidence accumulated which suggested a change in the host-parasite relationship. An important, if not the only, component of this change was a fall in the virulence or killing capacity of the virus. Strains of myxoma virus of five different levels of virulence had been recognized—the Australian standard laboratory strain, neuromyxoma (a greatly attenuated variant recovered in the laboratory), two slightly attenuated Australian field strains, and the strain which caused the outbreaks in Europe.

Professor Fenner's paper dealt with laboratory methods of recognizing slight differences in virulence, the changes in virulence which have occurred in the field in Australia, and experiments on the introduction of the European strain into Australia.

SECTION I: NUTRITION SUBSECTION.

Observations on Iron Absorption.

In a paper under the general heading of "Minerals in Nutrition", R. K. DOIG (Melbourne) said that current views on iron absorption suggested that iron was more readily absorbed in the ferrous state and that hydrochloric acid favoured the change from the ferric state and thus favoured absorption. Inferences respecting iron absorption had been made from balance studies, from observations on therapeutic results in iron-deficiency anæmia, from serial serum iron determinations and from studies on radioactive iron absorption. The present studies involved repeated observations on the serum iron levels following oral intake in seven healthy subjects, and numerous single determinations in a fistulous subject.

The results confirmed the slight difference in absorption in favour of ferrous iron over ferric iron. The data, however, did not confirm the view that absorption was altered by decrease in acidity of the gastric contents; and Dr. Doig suggested that iron absorption was probably related to upper intestinal function rather than to stomach function.

Trace Elements in Human Nutrition.

D. H. CURNOW (Perth) said that balance experiments over a thirteen-day period in a case of Wilson's disease (hepatolenticular degeneration) showed that on a daily intake of 4·0 milligrammes of copper 50% was being absorbed, and that the patient was in a positive copper balance of 0·7 to 0·8 milligramme per day. Administration of BAL and of "Versene" caused a rise in urinary copper excretion.

These results were discussed in terms of the mechanisms involved in the absorption and excretion of trace elements, and of their functions and interrelations.

SECTION N: PHYSIOLOGY AND BIOCHEMISTRY.

Proteolytic Activities of the Endocrine Glands.

W. G. LAVER and V. M. TRIKOJUS (Melbourne) reported that they had investigated and partially purified proteolytic enzymes in the thyroid, adrenal and pituitary glands. In the thyroid there were at least three proteolytic enzymes—a protease acting on hæmoglobin, thyroglobulin and other proteins at pH 3·5, and two peptidases, one active at pH 3·5 and the other at pH 7·8. The peptidase activity at pH 3·5 had been obtained practically free from protease activity and had been shown to possess the properties of a carboxypeptidase, splitting peptides with a protected α-amino group, such as N-acetyl-L-phenylalanyl-L-tyrosine, but having no action on peptides which did not have a free terminal carboxyl group, for example, phenylalanyl-L-tyrosyl amide. The other peptidase (pH 7·8) acted on simple peptides such as glycyl-leucine and leucyl-tyrosine. The protease had been purified about 600-fold and had been obtained practically free from peptidase activity (pH 3·5). The actions of the protease and peptidase (active at pH 3·5) on thyroglobulin, biologically labelled with I^{131}, had been compared.

No activation of the protease by thyroid-stimulating hormone or destruction of TSH by the protease at pH 3·5 had been observed.

In the adrenal gland, a protease active against hæmoglobin and with a pH optimum of 3·6 had been found and partially purified. This purified protease had been incubated with ACTH at pH 3·6, but no destruction of the hormone had been observed.

Studies of Vaginal Cornification in Vivo and in Vitro in Relation to the Local Action of Œstrogens.

J. D. BIGGERS and P. J. CLARINGBOLD (Sydney) reported that, following the administration of œstrogens either *in vivo* (systemically or locally) or *in vitro* in tissue culture, the first observable change in the vaginal epithelium was a sudden increase in the mitotic rate. This occurred twelve to eighteen hours after local administration or in tissue culture, but was delayed an additional six to twelve hours after systemic administration. Studies of the optimum conditions for local administration of œstrogens showed that a continual supply of œstrogen was required by the epithelium for mitosis to continue. Towards the end of the phase of increased mitotic rate the epithelium stratified and then keratinized. Early suggestions of the French school that natural œstrogens required metabolism before local action might be discounted, since it had been shown that the epithelium responded in tissue culture to these hormones.

Seasonal Changes in the Release of Antidiuretic Hormone in Response to Standard Heat Stimulus.

K. W. ROBINSON and W. V. MACFARLANE (Queensland) reported that four human subjects and one sheep had been subjected to control and to hot environment conditions at different seasons of the year. Heating was maintained at a standard level of 41° C.:31° C. (30 millimetres of mercury vapour pressure). It was found that the response at the end of four hours' heating in summer involved a hæmoconcentration of plasma proteins and a fourfold increase in the amount of antidiuretic substance released into the bloodstream. The antidiuretic material was assayed by intravenous injection into acol anæsthetized rats. During winter, heating to the same temperature (41° C.) as in summer produced neither blood concentration nor any significant amount of antidiuretic hormone. It was explained that this seasonal release of antidiuretic substances to hæmoconcentration stimulus meant that renal water loss was reduced in summer, and water was available for use in evaporative cooling. It was postulated that in summer intracellular water might be reduced and this might increase the readiness of release of ADH, as well as reducing the availability of intracellular water to prevent hæmoconcentration.

Some Aspects of the Regulation of Body Fluids.

T. E. LOWE (Melbourne) said that when patients, œdematous from congestive cardiac failure, were observed during the recovery period, and the body weight, fluid intake and fluid output were plotted daily, the resultant curves formed reproducible patterns.

It was believed that the body weight under the conditions of observation could be taken as an index of body fluid volume, and the volume/time curves so obtained could be divided into three portions: (*a*) an initial period of a few days in which the curve might rise, remain constant, or fall gradually; (*b*) a period, often as long as two weeks, in which there was a steady fall at first accelerating and then flattening out; and (*c*) a final period of several days in which the volume oscillated about a mean level. In each of these three phases study of the changes in free fluid intake and output indicated several patterns.

The observed behaviour of total fluid volume, intake and output of fluid could be predicted if the body was considered to regulate these variables on the basis of a continuous flow or "open" storage system of a fluid which was essentially a solution of electrolytes in water as a solvent. The controlling factors were thought to be the volume of some portion of the body fluid and the osmotic pressure of this fluid.

An analysis of this system and a comparison of predicted behaviour with clinical observations were made.

The Presence of Melanocyte Stimulating Hormone in the Human Pituitary Gland: Its Implication in Relation to Addisonian Pigmentation.

B. HUDSON and G. A. BENTLEY (Melbourne) reported that, until recently, the nature of the pigmentary disturbance that occurred in patients with Addison's disease lacked any physiological explanation. The hypothesis that this disturbance resulted from the abnormal or excessive secretion of a pituitary hormone was suggested by a number of clinical observations. Patients who were treated for prolonged periods with commercial corticotrophin not infrequently developed a mild pigmentary disturbance similar to that seen in Addison's disease. On the contrary, patients with destructive pituitary lesions showed abnormal pallor; and treatment of pigmented patients suffering from Addison's disease resulted in a decrease in pigmentation.

A hormone which stimulated the melanocytes of amphibia had been previously demonstrated in mammalian pituitary extracts. To the authors' knowledge this hormone had not been demonstrated previously in human pituitary extracts. If the hypothesis mentioned was to be upheld, the demonstration of this hormone was an essential observation. The authors' paper presented the data relevant to the extraction and assay of this hormone from fresh human pituitary tissue.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

BIRDS OF PORT JACKSON IN 1789.[1]

[From "A Narrative of the Expedition to Botany Bay", by Watkin Tench, Captain of Marines.]

To the naturalist this country holds out many invitations. Birds though not remarkably numerous are in great variety and of the most exquisite beauty of plumage: amongst which are the cockatoo, lory and perroquet: but the bird which chiefly claims attention is a species of ostrich approaching nearer to the emu of South America than any other we know of. One of them was shot at a considerable distance with a single ball by a convict employed for that purpose by the Governor: its weight when complete was seventy pounds and its length from the end of the toe to the tip of the beak seven feet two inches, although there was no reason to believe it had not attained its full growth. On dissection many anatomical singularities were observed: the gall bladder was remarkably large, the liver not bigger than

[1] From the original in the Mitchell Library, Sydney.

that of a farmyard fowl, and after the strictest search no gizzard could be found: the legs, which were of a vast length, were covered with thick strong scales, plainly indicating the animal to be formed for living amidst deserts: and the foot differed from that of an ostrich's by forming a triangle instead of being cloven. Goldsmith whose account of the emu is the only one I can refer to says "that it is covered from the back and rump with long feathers which fall backward and cover the anus: these feathers are grey on the back and white on the belly". The wings are so small as hardly to deserve the name and are unfurnished with those beautiful ornaments which adorn the wings of the ostrich: all the feathers are extremely coarse but the construction of them deserves notice—they grow in pairs from a single shaft, a singularity which the author I have quoted has omitted to remark. It may be presumed that these birds are not very scarce as several of them have been seen, some of them immensely large, but they are so wild as to make shooting of them a matter of great difficulty. Though incapable of flying, they run with such swiftness that our fleetest greyhounds are left far behind in every attempt to catch them. Their flesh was eaten and tasted like beef. Besides the emu many birds of prodigious size have been seen which promise to increase the number of those described by naturalists, whenever we shall be fortunate enough to obtain them. In the woods are various little songsters whose notes are equally sweet and plaintive.

Special Correspondence.

LONDON LETTER.

BY OUR SPECIAL REPRESENTATIVE.

RETURNING from the heat and humidity of New York, your correspondent found that the inhabitants of the British Isles had no complaints about the weather this summer, which was the best for seventy-five years. The warm dry summer was associated with a rise in the incidence of poliomyelitis, however, with the number of notifications around 4000, a figure higher than last year, but not comparable to the epidemic years 1947 and 1950. The proportion of non-paralytic cases to paralytic was about 50%, but the number of cases of bulbar poliomyelitis has not been excessive.

An outbreak of an infectious illness at first thought to be glandular fever also occurred this summer among the staff of the Royal Free Hospital, London. A large number of nurses were affected, some with neurological signs and symptoms, and the work of the hospital was interrupted as a result. An extensive investigation is proceeding to determine the causal agent of this mysterious illness presumed to be of viral origin.

Hospital Building.

An important announcement was made in June by the Minister of Health regarding the resumption of hospital building after an interval of sixteen years, which includes the war years.

No new hospital construction has been carried out since the hospitals in this country were taken over by the State in 1948, and the hospital authorities have had to "make do and mend" by stretching their resources to the uttermost. A sum of £60,000,000 has been spent on repairs, conversions and extensions to hospitals to enable them to meet the increasing demands.

In some areas the need for new hospitals is urgent owing to shifts in population and the creation of new towns. The hospitals to be built will not all be of a standard pattern, but will embody all that is best in design and construction, both in this country and abroad. For a period of the next three years it is the intention of the Minister to complete a number of projects, including the reconstruction of St. Thomas's Hospital (badly damaged during the war), the development of the Radcliffe Infirmary at Oxford, extensions to the General Infirmary at Leeds, a new teaching hospital for Sheffield, the development of Addenbrooke's Hospital at Cambridge and the first hospital for a new town at Harlow in Essex. In addition to this building programme, extensive schemes for replacement and conversion of plant in the majority of the teaching hospitals in this country are to be completed; this includes boiler plant, heating systems, and laundry and kitchen equipment.

Dental Health.

There is a new drive to provide better dental health for mothers and children. The incidence of dental disease is very high, and most young children suffer from decayed teeth. Undoubtedly the main cause of the increased dental decay in children is the greatly increased consumption of sweets. Investigation has shown that sugar taken at meal times has no appreciably harmful effects on the teeth. Studies in Sweden have shown conclusively that when sugar is eaten between meals there is an increase of dental decay. The real menace of sweets from the dental point of view is the constant sucking of lollies and other sweets, particularly last thing at night. Children aged five years have an average of five of their milk teeth missing, decayed or filled.

During the first five years of the National Health Service, about £400,000,000 was spent on the provision of artificial teeth. If this rate is maintained, it is estimated that one in six people in this country will be wearing full upper and lower dentures in a few years' time. The loss of teeth and their replacement by dentures have come to be regarded as inevitable by the majority of people, although dental disease is largely preventible by personal home care.

Help for Malta.

In response to an urgent appeal by the Government of Malta, an agreement has been reached for the treatment of between 100 and 200 tuberculosis patients in English hospitals. This has been made possible by the steady fall in the number of new cases of tuberculosis in England. The Maltese Government will send over with the patients medical officers for training and the necessary nursing and other staff, and will defray the cost of treatment.

Consultants and Income Tax.

A recent decision of the Income Tax Commissioners has seriously disturbed consultants in the National Health Service, the British Medical Association and the Medical Defence Societies. This decision brings about a change in the method of assessment of income derived from appointments at hospitals under the National Health Service. Of the 6000 or 7000 consultants who work in the hospitals, the majority are engaged on a part-time basis, the remaining portion of their time being for private work. In many cases, the income derived from hospital work represents the major part of the consultants' income, and the decision of the income tax authorities is based on the assumption that the hospital (or public) work of a part-time consultant is "an employment" for the purposes of the income tax Acts. They contend that the part-time consultant is engaged under a contract of service, which gives rise to the legal relationship of master and servant, and that the form of assessment relating to employees generally should apply. The consultants, however, do not accept the view that the consultant is an employee and contend that he is one who practises a profession. It is feared that the action of the income tax authorities may represent an insidious step towards the introduction of a whole-time salaried service, a form of service to which the whole profession is strongly opposed. The consultants, through the British Medical Association, intend to test the validity of the action of the Income Tax Commissioners in the courts, and test cases are in preparation.

Correspondence.

THE PENSIONER MEDICAL SERVICE.

SIR: I have read with considerable interest the leading article on the Pensioner Medical Service in the journal of October 29, 1955. I am sure that most people in Australia today will agree with your view that it "is a service worthy of respect which should be cherished and maintained at the highest possible ethical level". It would indeed be a tragedy if the service were destroyed by unethical practices. Many instances of serious abuse have been uncovered and punished, largely as a result of the activities of the Committees of Inquiry. However, much yet remains to be done to free the service from the abuse that is still threatening to destroy it.

It will no doubt be of interest to your readers to learn that further steps have recently been taken to combat this abuse by introducing several amendments into the *National Health Act*.

The valuable deterrent effect of publicizing penalties imposed under the Act is recognized. Up to the present it

has been permissible to notify in the *Commonwealth Gazette* only those cases where the Minister has reprimanded a doctor or chemist; has terminated his Pensioner Medical Service agreement; or has revoked his approval to supply, or authority to write, prescriptions for pharmaceutical benefits following a Committee of Inquiry report into a case of suspected abuse. My policy has been to notify the action taken in all such cases except where a committee has recommended against publication.

Although the Act authorized reduction or disallowance of a doctor's claim under the Pensioner Medical Service on the recommendation of a Committee, it did not permit publication of such action. However, this has now been rectified and power has been taken to notify in the *Gazette* the names of the doctors concerned in these cases. Provision has also been made to publish the fact that a doctor or chemist has been suspended pending court proceedings or following conviction in a court case.

In some States, the Medical Services Committees of Inquiry established under the Act have been unable to cope with the number of cases requiring their attention. As a result it has not been possible to refer to these committees all the cases that would otherwise have been referred to them for inquiry and report. The Act has, therefore, been amended to provide for the establishment of additional Committees of Inquiry where necessary. Provision has also been made for the employment of a medical consultant in special cases where an expert medical opinion on the necessity for the treatment given to the pensioner is considered to be desirable.

Whilst elimination of abuse is dependent on the maintenance of the highest ethical standards by all concerned, it is hoped that these special measures will curb the activities of those who fail to measure up to the required standards.

Yours, etc.,

Parliament House, Canberra,
November 2, 1955.

EARLE PAGE.

USE AND ABUSE OF BLOOD TRANSFUSIONS.

SIR: At the meeting of the New South Wales Branch of the British Medical Association held on June 30 last, comment was made on the increasing frequency of severe phlebitis in connexion with intravenous saline therapy. It was suggested that some irritant derived from the rubber tubing employed might be the cause. Other possible reasons exist, however. There is a suspicion that the pH of the solutions available is subject to undesirable variation, or that contamination by impurities derived from their glass containers may occur. The matter is serious enough to warrant attention by the manufacturers of these products.

Yours, etc.,

143 Macquarie Street, Sydney,
September 26, 1955.

S. V. MARSHALL.

A NEW APPROACH TO OPERATIONS FOR PROLAPSE.

SIR: I feel it is necessary to reply to the article of Dr. J. Cameron Loxton which appeared in your journal of September 17, 1955.

As a former R.M.O. and S.R.O. of the Jessop Hospital for Women, Sheffield, during the years 1921 and 1922 I had the good fortune of being associated with Professor Miles Phillips, the late W. W. King and John Chisholm. All these were members of the North of England Gynæcological and Obstetrical Society, contemporaries and students of Donald and Fothergill. Further, they had the unique advantage of assisting and watching Donald and Fothergill at Saint Mary's Hospital, Manchester. Thus the operation for utero-vaginal prolapse which they used could be termed the original Manchester operation.

Now Dr. Loxton states that the Manchester operation "can no longer hold its former place . . ." (and) must give way to more mechanically sound and scientific methods. For this rather rash statement he advances many reasons, *inter alia* "a predisposition towards fresh prolapse . . . such as enterocele and urethrocele", and narrowing of the vaginal vault rendering coitus either painful or impossible.

In the operative treatment of utero-vaginal prolapse the Manchester operation presents certain principles of treatment which even today are recognized as of paramount importance—namely, the upward dislocation of the bladder, cervical amputation and shortening of Mackenrodt's ligaments (or parametria, as the Manchester School preferred to call these) in front of the cervix. This was preceded by a careful pelvic examination and a cervical dilatation and, if considered necessary, a curettage; a pre-operative history excluded stress incontinence, and the examination will demonstrate the possibility of a cul-de-sac hernia. The Sheffield gynæcologists, in my time, always operatively explored the pouch of Douglas, if this was considered herniated, and treated it by excising excess peritoneum and suturing the utero-sacral ligaments together.

If a cul-de-sac hernia and/or a urethrocele occurs after a Manchester operation, then either the gynæcologist has failed to recognize their presence or else they have not yet developed; they cannot be ascribed as a failure of the Manchester operation, which deals with neither of these pathological processes.

In regard to the possibility of a narrowed vagina after the operation, let me quote the following statements by Wilfred Shaw (1954): "In Great Britain the majority of surgeons favour the Fothergill procedure . . . the vagina is not shortened and it is rare for a hernia of the pouch of Douglas to develop after the operation"; and later: "This operation introduced by Donald and Fothergill gives extremely good results in selected cases. Most surgeons use their own modification of the original Fothergill technique."

I never saw this happen either in Sheffield or in my cases. The technique of its prevention is clearly described by Malpas (1955). Malpas states that "there is general agreement that the standard operation for postural prolapse is the Fothergill operation". Undoubtedly many gynæcologists use variations of technique in the Manchester operation—a Sturmdorff suture may be used in the cervix, Wilfred Shaw presents a special suture for anchoring the bladder to the cervix, others may prefer a preliminary vertical incision in the anterior vaginal wall, others may prefer to dissect the "pubo-cervical fascia" from the vagina and later suture it to support the dislocated bladder in its new position, but the principles enunciated by Donald and Fothergill are always used.

With due respect I suggest that, whilst Dr. Loxton has described to us some slight variations of technique, he has not departed from the principles of the Manchester operation, which he apparently considered out of date.

Yours, etc.,

4 Robey Street, Mascot, New South Wales.
October 17, 1955.

C. H. JAEDE.

References.

SHAW, WILFRED (1954), "Text Book of Operative Gynæcology", E. and S. Livingstone, 236.

MALPAS, PERCY (1955), "Genital Prolapse", in "British Obstetrical and Gynæcological Practice", edited by Eardley Holland and Aleck Bourne, William Heinemann, 2: 580.

SIR: The article by J. C. Loxton in a recent journal and the comment by Chapman is of great interest to one who has for years felt that vaginal hysterectomy was an operation of great value. My personal experience of the procedure would be little less than 400 cases, and the vast majority of these patients have been seen at varying intervals up to fifteen years, so assessment of results has been reasonably adequate. Criticism of the operation has, I feel, frequently emanated from those whose experience in the field has been limited.

Mr. Loxton's paper, however, in my opinion, is perhaps intentionally provocative. It is indeed a courageous English or Australian surgeon who preaches the dictum of many American gynæcologists who maintain that the real cure of a second degree prolapse necessitates vaginal hysterectomy. Mr. Chapman's comments are more modified and in accord with my own. In the absence of enterocele or uterine pathology I, as yet, treat very few cases of prolapse by vaginal hysterectomy and repair. Over the past fifteen years I have been a little impressed that the ultimate result in vault security has been better after vaginal hysterectomy than after the Manchester operation, but to date remained unconvinced. There is no question that enterocele will be seen to occur more frequently after the Manchester operation, but in the majority of cases I would feel that this is due to failure to recognize the presence of a small herniation when the operation was performed, and this can scarcely be a criticism of the Manchester operation.

Mr. Loxton's paper does stress the importance of a thorough appreciation of the anatomy of the pelvic sup-

ports in the performance of any repair, and in this he is to be lauded. I also appreciate his attitude towards conservation of vaginal mucous membrane, but this is of equal importance in any repair. I cannot agree with him in his suggestion that the Manchester operation is so much more likely to lead to a narrow foreshortened vagina; for, providing adequate mucous membrane is retained and the perineum not advanced, the vagina after a Manchester operation should be adequate. There is no doubt that the more recent technique for vaginal hysterectomy has very largely eliminated the old criticism of the operation—that it left a short vagina.

In conclusion, as a proponent of vaginal hysterectomy, I would compliment Mr. Loxton on his paper; and if to be provocative was to some extent his aim, I trust that by so doing he has stimulated further interest in what is undoubtedly an excellent operation.

Yours, etc.,

179 St. George's Terrace, HUGH C. CALLAGHER.
Perth,
October 17, 1955.

SEVERE REACTION FOLLOWING PENICILLIN INJECTION.

SIR: Whilst reading a letter published in THE MEDICAL JOURNAL OF AUSTRALIA of August 13, 1955, under the pen of Dr. F. Walton, of Wollongong, it occurred to me that it might be of interest to Dr. Walton and perhaps to others to hear what occurs at the 97th General Hospital, Frankfurt, Germany; because this is also indicative as to what procedures are adopted in America. The 97th General Hospital is situated at Frankfurt, Germany, and is the centre for all serious or obscure cases occurring in United States Army forces not only in western Germany but in Europe.

During the past year it has been my good fortune to have access to the wards, operating rooms and lecture theatres of this institution; this I attribute to the fact that I was for a time in the 1939 war closely associated with American medical units; but chiefly to the high esteem in which all Australians are held by these soldiers, who have fought and associated with our troops in the 1939 war and more recently and extensively in Korea. Particularly in Korea did our troops build up the reputation of Australia.

Most of us when first using penicillin regarded it as a safe form of medication. Gradually that state has changed, and evidence is now available to prove that in many cases it cannot be so regarded. During the first nine years that penicillin was in use only two fatal reactions were reported in medical literature. In an eighteen-monthly period commencing March, 1952, Kern and Wimberley (1953) showed that there occurred 17 anaphylactoid deaths. In a survey made by Welch and his co-workers (1953) covering 95 general hospitals situated in 11 United States cities with a total bed capacity of 51,000 beds—this is 7·5% of hospital beds in the United States of America—it was shown that in the preceding two years 59 anaphylactoid reactions to penicillin were reported, of which 19 were fatal. Special attention was called to the fact that of the 59 reactions 55 were in connexion with procaine penicillin; and that of the 19 deaths 18 were also in relation to procaine penicillin.

In the United States of America area of Germany there have been at least six deaths following the administration of penicillin, and of these four have been of the anaphylactoid type. I have not personally seen these cases, but am indebted to Colonel Biedermann, M.C., for the above figures. Amongst severe reactions seen by me was one case of intensive œdema to the uvula following penicillin.

Bearing in mind the above facts, particular attention is paid to the taking of the history in relation to: (i) any previous use of penicillin, (ii) reactions during any previous course of penicillin, (iii) the presence of any allergy in either personal or family history. Particular caution is advised in the use of long-acting penicillin preparations. Reactions are much more common with procaine penicillin than with aqueous, and also the danger is greater once the reaction starts.

The following procedures are stressed at 97th General: (i) Test for sensitivity to penicillin in any questionable case. Details below. (ii) Give the injection, or at least the initial one of the series, in the arm, or at a point low enough to allow the application of a tourniquet should a serious reaction occur. (iii) Have readily available the means to combat an accelerated anaphylactoid type of reaction—namely: dry sterile syringes (two cubic centimetres, 10 cubic centimetres and tuberculin), epinephrine injections 1:1000, aminophyllin injection, tourniquet, oxygen and suitable apparatus for its administration, epinephrine in oil, nor-epinephrine, ephedrine *et cetera*, antihistamine drugs, both oral and parenteral, ACTH and cortisone, sedative and hypnotic drugs.

Details of skin testing used at 97th General Hospital, United States Army, Western Germany—this is used in any questionable case:

Test for sensitivity to Penicillin in any questionable case.

Aqueous Crystalline Penicillin. Make a solution containing 1000 units per cubic centimeter by dilution with sterile distilled water. Using a tuberculin syringe, inject 0·1 c.c. of this solution intradermally on the flexor surface of the forearm. A positive "accelerated" reaction is indicated by a flare of erythema, local itching (and occasionally by such subjective symptoms as weakness, syncope, and shortness of breath) within 30 minutes.

Procaine. A similar intradermal test may be made by injecting 0·1 c.c. of 1 per cent. procaine solution as described above.

Procaine and Other Long-Acting Penicillins. Place a drop of the preparation to be used upon a superficial scratch on the skin of the forearm. Hypersensitivity may be indicated by an itching wheal within 30 minutes.

Systemic Tests. If the intradermal or the scratch test as described above is negative, inject a small dose of the preparation to be used in the way it will be used. Prior to intravenous medication with Penicillin, inject intravenously no more than 100 units of the make and lot number selected, keep the patient under continuous observation, and have the means on hand to offset, if possible, a shock-like episode. Under urgent circumstances, this procedure may be used even if the skin test or history is positive. The first injection of a long-acting penicillin preparation should be given at a reduced dosage (100 to 1000 units roughly estimated) at a location and with the precaution previously described.

Whether or not sensitivity tests are performed, the patient should be observed closely for at least 30 minutes following the first injection of a series. Oral Penicillin appears much less likely to cause reactions of the immediate type than Penicillin administered parenterally. However, patients given oral Penicillin should be cautioned to report immediately any unusual symptoms which occur.

Yours, etc.,

R. V. BRETHERTON, M.B., B.S. (Melb.).
Hanau a. Main,
Cranachstrasse 1-5,
Germany.
October 12, 1955.

References.

KERN, R. A., and WIMBERLEY, N. A., JUNIOR (1953), "Penicillin Reactions: Their Nature, Growing Importance, Recognition, Management and Prevention", *Am. J. M. Sc.*, 226: 357.

WELCH, H., LEWIS, C. N., KERLAN, I., and PUTAM, I. E. (1953), "Anaphylactic Reactions to Penicillin", *Antibiotics & Chemother.*, 3: 891; Editorial, *New England J. Med.*, 249: 998.

THE MANAGEMENT AND TREATMENT OF THE CHRONIC ASTHMA PATIENT.

SIR: With reference to statements relating to an activity of the New South Wales Department of Public Health appearing in THE MEDICAL JOURNAL OF AUSTRALIA of October 8, 1955, at page 590, it appears desirable to offer some comment.

Owing to concern at the amount of ill health caused by bronchial asthma in children of school age and the apparent ineffectiveness of their treatment in many cases, this department some years ago decided to investigate a method of treatment and prevention developed by the late Dr. R. J. N. Whiteman, of Sydney. Parents of a number of asthmatic children were invited to cooperate by permitting their children to join an experimental group under the charge of the School Medical Service of the New South Wales Department of Public Health. In association with medical officers of that department, Dr. Whiteman generously agreed to supervise the experiment, which is now approaching completion, notwithstanding a temporary setback caused by the regretted and untimely death of Dr. Whiteman.

The results, as assessed by the department, are set out in the following summarized preliminary statement. Two groups of children under the treatment, 145 in all, of whom the majority were aged six to ten years, were specially followed up over a period of two years by the department's medical staff. At the end of that time they were classified into five categories, viz.: (i) those having no attack of asthma or bronchitis since beginning treatment, 61; (ii) one slight attack only, all other symptoms much improved, 53; (iii) no attack in the concluding six months, all other symptoms improved, 18; (iv) still some slight attacks, all other symptoms improved, 9; (v) not improved, 4. Comparison of the two groups shows that the observed results were similar in each group. Photographic records indicate the steady improvement in physique which accompanied successful treatment. It should be mentioned that no surgical treatment is employed.

Claims of such results might at first sight appear to be excessive. However, the department's records are available to any unprejudiced medical investigation. In justice to the late Dr. Whiteman the New South Wales Department of Public Health would welcome such inquiry.

Yours, etc.,
H. G. WALLACE,
Director-General of Public Health,
New South Wales.

52 Bridge Street,
Sydney,
October 17, 1955.

THE CLASSICS AND MEDICINE.

SIR: Perhaps mine is "a voice crying in the wilderness", but I wish to support the contention expressed in the letter from your correspondent, J. M. A. Lowson (October 15, 1955). Fundamentally, I presume, leuchæmia (or leukæmia) is derived from λευκ- and αἰμ-—"white blood".

One would suppose, therefore, that the aspirate should also be retained in anæmia—thus anhæmia—in order to be consistent.

Yours, etc.,
W. KEITH MYERS.

135 Macquarie Street,
Sydney,
October 18, 1955.

REDUCTION OF INTUSSUSCEPTION BY BARIUM ENEMA.

SIR: I would like to clarify a statement made by Dr. G. R. Silvester, reported on page 572 of THE MEDICAL JOURNAL OF AUSTRALIA, October 8, 1955, in which he states: "He never exceeded a screening time of twenty minutes, and the period was usually between ten and fifteen minutes."

The examination may take an overall time of twenty minutes and certainly cannot mean tube operating time, as *some may think.*

In any fluoroscopic examination the objective is to deliver the minimum possible dose of X rays consistent with the carrying out of the required procedure by intermittent flashes for observation. The sum total of these intermittent flashes should not exceed several minutes at most, for the following reason, that the "dose rate in roentgens per minute" varies in every X-ray machine, and what may be a "safe" total screening time for one machine may be extremely dangerous in another.

Tests of 117 fluoroscopes made by B. P. Sonnenblick in 1952 showed a variation between 2*r* and 118*r* per minute, and 20% of the machines exceeded 30*r* per minute during routine screenings. The maximum gonad dose is considered to be 75*r*, and at least twenty-one days should elapse before there is any further exposure to X rays.

Any general statement in regard to "safe" screening time should be qualified by the technical factors of kilovoltage, distance, current, total filtration, area of examination, and the estimated skin dose per minute at the settings of the particular machine used.

Yours, etc.,
D. G. MAITLAND.

147 Macquarie Street,
Sydney,
October 27, 1955.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Appointment.

THE Post-Graduate Committee in Medicine in the University of Sydney announces the appointment of Dr. J. Colvin Storey as Intern Warden. His duties will be to inquire and report to the Post-Graduate Committee on all aspects of the training of young graduates in the hospitals of New South Wales during their first and second years after graduation, including the allocation of positions, their training programmes and training facilities, and their problems at the conclusion of their intern years, to advise interns generally and to advise the committee on hospitals and other matters relating to training for general practice.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 52, of October 20, 1955.

AUSTRALIAN MILITARY FORCES.

Australian Regular Army.

Royal Australian Army Medical Corps.

The notification respecting 2/40135 Captain J. V. C. Brassil which appeared in Executive Minute No. 127 of 1955, promulgated in *Commonwealth Gazette* No. 35 of 1955, is withdrawn.

2/40135 Captain J. V. C. Brassil is transferred to the Citizen Military Forces, Royal Australian Army Medical Corps (Medical) (Eastern Command), 20th May, 1955, with regimental seniority in accordance with his Army seniority (19th May, 1953).

Citizen Military Forces.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—The provisional appointment of 2/56843 Captain A. H. Gibson is terminated, 25th July, 1955. To be Captain (provisionally), 26th July, 1955: 2/56843 Alan Hugh Gibson.

2/242959 Captain J. V. C. Brassil is transferred from the Australian Regular Army, Royal Australian Army Medical Corps (Medical), 20th May, 1955, with regimental seniority in accordance with his Army seniority (19th May, 1953). 2/130113 Captain (provisionally) E. A. Lennon relinquishes the provisional rank of Captain and is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Eastern Command) in the honorary rank of Captain, 1st August, 1955. To be Captain (provisionally), 14th September, 1955: 2/108252 Desmond Patrick Clarke.

Southern Command.

Royal Australian Army Medical Corps (Medical).—3/101834 Honorary Captain B. W. Fox is appointed from the Reserve of Officers, and to be Captain (provisionally), 26th July, 1955.

The provisional appointment of 3/101823 Captain K. H. McLean is terminated, 1st April, 1955. To be Lieutenant-Colonel, 1st July, 1955: 3/50196 Major (Temporary Lieutenant-Colonel) C. D. Donald. To be Captain (provisionally), 2nd April, 1955: 3/101823 Kenneth Hay McLean.

3/101011 Captain C. W. E. Wilson is seconded whilst undergoing post-graduate studies in the United Kingdom, 20th June, 1955. 3/101023 Captain (provisionally) K. J. Neerhut relinquishes the provisional rank of Captain and is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Southern Command) in the honorary rank of Captain, 15th August, 1955.

Central Command.

Royal Australian Army Medical Corps (Medical).—4/35233 Lieutenant-Colonel J. D. Rice relinquishes command of 1st Casualty Clearing Station, 23rd August, 1955. 4/31903 Lieutenant-Colonel C. M. Gurner relinquishes command of 3rd Field Ambulance, 23rd August, 1955, and is appointed to

command 1st Casualty Clearing Station, 24th August, 1955. 4/31904 Major P. S. Eyles is appointed to command 3rd Field Ambulance, and to be Temporary Lieutenant-Colonel, 24th August, 1955. 4/32015 Captain (provisionally) W. D. Proudman is seconded whilst in the United Kingdom, 19th September, 1955.

Tasmania Command.

Royal Australian Army Medical Corps (Medical).—6/15416 Captain (provisionally) A. J. Foster relinquishes the provisional rank of Captain, and is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Tasmania Command) in the honorary rank of Captain, 14th August, 1955.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps.

Northern Command.—The resignation of Honorary Captain J. J. Power of his commission is accepted, 1st August, 1955.

To be Honorary Captains, 2nd September, 1955.—Keith Eliott Hirschfeld, Marceline Dorothy Victoria Pickup, Hugh Alexander Urquhart, and Ronald Ian Waugh.

To be Honorary Captain, 27th July, 1955.—Graham Melrose Windrum.

Eastern Command.—To be Honorary Captains: Ronald Robert Fitzgerald, 14th June, 1955, Rowland Gordon Elmslie, 18th July, 1955, Kenneth Sidney Cranney, 18th July, 1955, and Gordon James Ormandy, 8th August, 1955.

Southern Command.—Honorary Captain W. M. Box is retired, 26th August, 1955.

To be Honorary Captains.—Stanley Caldwell Berger, 18th July, 1955; Alexander John Mitchell, 20th July, 1955; and Henry Ralph Johnson and Walter Ian Harewood Johnston, 15th August, 1955.

Royal Australian Air Force.

Permanent Air Force: Medical Branch.

Andrew Mackinnon Muirhead (042575) is appointed to a short-service commission, on probation for a period of twelve months, 15th August, 1955, with the rank of Flight Lieutenant.

The probationary appointment of the following Flight Lieutenants is confirmed: B. A. Hintz (014532), D. N. Bennett (039747).

The following Squadron Leaders are appointed to a permanent commission: R. H. B. Sacks (036080), 19th November, 1955; P. A. O'Brien (035952), 21st November, 1955.

Active Citizen Air Force: Medical Branch.

The appointment of Flight Lieutenant (Temporary Wing Commander) C. A. Frew (021931) is terminated, 31st August, 1955, on demobilization.

Air Force Reserve: Medical Branch.

The following former officers are appointed to a commission with rank as indicated: (Squadron Leader) G. A. Leyland (043897), 10th September, 1955; (Flight Lieutenant (Temporary Wing Commander)) C. A. Frew (021931), 1st September, 1955; (Flight Lieutenent) J. J. Bain (0210563), 23rd July, 1955.

Royal Australasian College of Surgeons.

FINAL FELLOWSHIP EXAMINATION.

THE next meeting of the Court of Examiners of the Royal Australasian College of Surgeons for the final examination for Fellowship of the College will be held at the College in Melbourne, beginning on Friday, May 4, 1956. Candidates who desire to present themselves at this examination should apply, on the prescribed form, to the Censor-in-Chief for permission to do so before March 22, 1956. The appropriate forms are available from the Secretary, Royal Australasian College of Surgeons, Spring Street, Melbourne, C.1.

Candidates who have already been approved by the Censor-in-Chief but who have not yet presented for the examination may present at this examination, provided they notify the Secretary of their intention to do so by March 22, 1956. It is emphasized that entries close on this date and that late entries cannot be accepted.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED OCTOBER 22, 1955.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	2	2(1)	3(2)	..	2(1)	..	3	..	12
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	3	..	..	..	..	..	3
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	1	..	..	..	..	..	..	1
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	5	23(19)	5(4)	..	..	..	..	4	37
Diphtheria	4(1)	4(3)	1(1)	..	3(3)	..	..	..	12
Dysentery (Bacillary)	..	..	3(2)	..	1(1)	..	..	..	4
Encephalitis	1(1)	1(1)	..	1	..	..	..	..	3
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	44(21)	73(34)	..	6(4)	3(3)	2	..	3	131
Lead Poisoning	..	..	1	..	..	..	..	..	1
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	..	..	..	..	..	..	..
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	3(2)	5(4)	2	1(1)	..	..	..	..	11
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	..	..	2(1)	..	..	..	..	2
Puerperal Fever	..	..	1(1)	..	..	..	..	..	1
Rubella	..	80(46)	..	3(2)	1	..	..	..	84
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	10(7)	17(7)	28(8)	7(5)	..	..	..	1	63
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	1(1)	..	..	..	..	..	..	1
Trachoma	..	..	..	..	18(1)	..	..	..	18
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	65(48)	10(6)	13(10)	9(5)	7(5)	6	2	..	112
Typhoid Fever	..	2(2)	1(1)	..	..	..	..	..	3
Typhus (Flea-, Mite- and Tick-borne)	..	..	1	..	..	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

The examination fee is £21, *plus* exchange on cheques drawn on banks outside Melbourne, and must be paid to the Secretary by March 22, 1956.

The examination will be conducted in general surgery and in the special branches of ophthalmology, laryngo-otology, gynæcology and operative obstetrics, orthopædics, urology, neurosurgery and thoracic surgery.

Congresses.

AUSTRALASIAN CARDIAC SOCIETY.

THE annual meeting of the Australasian Cardiac Society will be held in Wellington, New Zealand, during the week commencing Sunday, March 25, 1956. This follows the meeting of The Royal Australasian College of Physicians. The honorary secretary of the Australasian Cardiac Society is Dr. E. F. Gartrell, 172 North Terrace, Adelaide.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST.

THE fourth International Congress on Diseases of the Chest will be held at Cologne, Germany, from August 19 to 23, 1956. It is sponsored by the Council on International Affairs of the American College of Chest Physicians with the cooperation of the Federal Republic of Germany. Further information may be obtained from the American College of Chest Physicians, 112 East Chestnut Street, Chicago II, Illinois, United States of America.

SECOND EUROPEAN CONGRESS OF CARDIOLOGY.

THE second European Congress of Cardiology will take place at Stockholm, Sweden, from September 10 to 14, 1956, under the presidency of Professor Gustav Nylin.

The preliminary programme for panel discussions and round table conference has been made up. The subjects for panel discussions will include the ætiology and pathogenesis of atherosclerosis, isolated atrial and ventricular septal defects, pulmonary hypertension, cardiac output and its regulation, acquired aortic stenosis, circulation in hypothermia, and organic peripheral arterial disease. Round table conferences will be held on the treatment of essential hypertension, the treatment of paroxysmal arrhythmias and other ectopic rhythms, phonocardiography, and the indications and hazards of heart catheterization and angiocardiography. Another item to be discussed will be the applicability of the röntgenological heart volume determination.

The congress will be open in the first place to members of the national societies of cardiology affiliated to the European Society of Cardiology. As far as space permits, it will also be open to other doctors interested in cardiology, both within and outside Europe. Speakers at the panels and round table conference will be elected by invitation.

The secretary-general of the congress is Dr. Karl Erik Grewin, Södersjukhuset, Stockholm S, Sweden.

Medical Appointments.

Dr. William Cotter Burnell Harvey and Dr. Charles James Officer Brown have been reappointed members of the Advisory Council, created under provisions of the *Tuberculosis Act*, 1948, for a further period of three years from September 1, 1955.

Dr. R. C. Angove has been appointed honorary assistant physician at the Royal Adelaide Hospital.

Professor W. V. MacFarlane has been appointed a member of the Council of the Queensland Institute of Medical Research.

Dr. J. H. Kneebone has been appointed registrar in the maternity section, The Queen Elizabeth Hospital, South Australia.

Dr. J. G. Reid has been appointed registrar in the maternity section, The Queen Elizabeth Hospital, South Australia.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Christie, Gwenda Joy, M.B., B.S., 1954 (Univ. Sydney), 9 Somerville Street, Arncliffe, New South Wales.

Patterson, Robert William, M.B., B.S., 1954 (Univ. Sydney), 10 Court Street, Parkes, New South Wales.

Deaths.

THE following deaths have been announced:

MUNDAY.—Neill Horace Munday, on October 25, 1955, at Adelaide.

ROBINSON.—George Seaborne Robinson, on October 24, 1955, at Melbourne.

Diary for the Month.

Nov. 14.—Victorian Branch, B.M.A.: Finance Subcommittee.
Nov. 15.—New South Wales Branch, B.M.A.: Medical Politics Committee.
Nov. 16.—Western Australian Branch, B.M.A.: General Meeting.
Nov. 17.—Victorian Branch, B.M.A.: Executive of Branch Council.
Nov. 17.—New South Wales Branch, B.M.A.: Clinical Meeting.
Nov. 22.—New South Wales Branch, B.M.A.: Ethics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all contract practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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